Socio-emotional cognition and autism spectrum disorder symptoms in anorexia nervosa

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Thesis submitted for degree of Doctor of Philosophy (PhD)

2020

Abstract

Anorexia nervosa (AN) is a severe eating disorder (ED) characterised by high mortality rates and substantial functional impairment. Theoretical models of AN have proposed that interpersonal difficulties are key to the development and maintenance of the disorder. However, the mechanisms underlying these social difficulties are poorly understood. While some research has demonstrated difficulties in empathy, understanding of nonverbal communication, and social attention in individuals with AN, evidence is inconsistent. At the same time, there is evidence to suggest a relationship between AN and autism spectrum disorder (ASD), with a significant proportion of individuals with AN showing high levels of ASD symptoms. Given that difficulties in social communication and understanding are core characteristics of ASD, it is possible that variations in ASD symptoms are associated with differences in social cognition in individuals with AN.

Thus, the overall aim of the thesis is to investigate the impact of ASD symptoms on socio-emotional cognition in adults in the acute and recovered stages of AN, compared to healthy controls (HCs). The first few studies focus on exploring comorbid ASD symptoms in AN, while the latter part of the thesis examines performance in a variety of socio-emotional domains, specifically empathy, perception of nonverbal communication, and social attention.

The findings demonstrate that around one quarter of individuals in the acute and recovered stages of AN display high levels of ASD symptoms, suggesting that ASD symptoms may be relatively independent from clinical state. Generally, only small differences in socio-emotional cognition were found in those with AN. Specifically, lower positive affective empathy and reduced attention to faces was found in individuals with AN compared to recovered AN and HCs. Overall, ASD symptoms were better predictors of socio-emotional abilities than ED status; high ASD symptoms predicted lower cognitive and affective empathy abilities, emotion recognition performance, and attention to faces, while controlling for group membership.

The results demonstrate the importance of clinical heterogeneity within the overall diagnosis of AN, suggesting that those with high ASD traits may show particular difficulties in socio-emotional cognition. Different treatment approaches or adaptations to treatment may be required for this subgroup of patients. Future work should directly compare indices of social cognition in individuals with AN to those with a diagnosis of ASD, in order to elucidate potential transdiagnostic factors responsible for social difficulties across disorders.

Acknowledgements

I would firstly like to thank my supervisors Professor Kate Tchanturia and Dr Amy Harrison. It has been a privilege to work with such intelligent and inspiring mentors, and I am extremely grateful for the support, guidance, and opportunities you have given me throughout my PhD.

I would also like to thank my parents, who have consistently believed in me and supported me through my education and academic career. You have been a great source of confidence and encouragement. I would also like to give a huge thanks to my friends. Their stimulating company and unwavering belief in me has truly helped me push through all the late nights.

Finally, I would like to thank all of the participants who took part in the research for giving up their time to help me. I wish you all the very best for the future.

Financial acknowledgements

The work conducted for this thesis was funded by a studentship provided by the Economic and Social Research Council (ESRC), and the Psychiatry Research Trust.

List of abbreviations

3Di-sv	Developmental Diagnostic Dimensional Interview-short version
ABMT	Attentional bias modification treatment
ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
ADOS-2	Autism Diagnostic Observation Schedule, 2nd edition
AN	Anorexia nervosa
AN-BP	Anorexia nervosa, binge-eating/purging subtype
ANOVA	Analysis of variance
AN-R	Anorexia nervosa, restricting subtype
AN-WR	Anorexia nervosa, weight restored
AOI	Area of interest
APA	American Psychiatric Association
AQ	Autism Quotient
AQ-10	Autism Quotient, abbreviated version
ASD	Autism spectrum disorder
BD	Bipolar disorder
BDD	Body dysmorphic disorder
BED	Binge eating disorder
BES	Basic empathy scale
BMI	Body mass index
BN	Bulimia nervosa
BPD	Borderline personality disorder

CBT	Cognitive behavioural therapy
CI	Confidence interval
cm	Centimetres
CNWL	Central and North West London
CREST	Cognitive remediation and emotion skills training
CRT	Cognitive remediation training
CS	Correlation stability
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EC	Empathic concern
ED(s)	Eating disorder(s)
EDE-Q	Eating Disorder Examination Questionnaire
EDI	Eating Disorder Inventory
EI	Expected influence
EMDR	Eye movement desensitisation and reprocessing
EMG	Electromyography
EQ	Empathy Quotient
FEF	Frontal eye fields
FET	Films expression task
FS	Fantasy
GABA	γ-aminobutyric acid
GAD	General anxiety disorder
HADS	Hospital anxiety and depression scale
HADS-A	Hospital anxiety and depression scale, anxiety subscale

HADS-D	Hospital anxiety and depression scale, depression subscale
HC(s)	Healthy control(s)
Hz	Hertz
I_7	Impulsiveness, venturesomeness, and empathy questionnaire
IBW	Ideal body weight
ICD	International Classification of Diseases
IoPPN	Institute of Psychiatry, Psychology, and Neuroscience
IQ	Intelligence quotient
IQR	Interquartile range
IRI	Interpersonal Reactivity Index
KCL	King's College London
LASSO	Least absolute shrinkage and selection operator
LSAS	Liebowitz Social Anxiety Scale
M	Mean
MANTRA	Maudsley model of anorexia nervosa treatment for adults
MDD	Major depressive disorder
MEG	Magnetoencephalography
MET	Multifaceted Empathy Test
MiniPONS	Mini Profile of Nonverbal Sensitivity
ms	Milliseconds
MSPSS	Multidimensional Scale of Perceived Social Support
n	Sample size
NAcc	Nucleus accumbens

NES	Night eating syndrome
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPV	Negative predictive value
OCD	Obsessive compulsive disorder
OFC	Orbitofrontal cortex
OSFED	Otherwise specified feeding or eating disorder
PD	Personal distress
PPV	Positive predictive value
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PT	Perspective taking
RCT(s)	Randomised controlled trial(s)
REC	Recovered anorexia nervosa
RMET	Reading the Mind in the Eyes Test
RRB	Restrictive and repetitive behaviour
RT(s)	Reaction time(s)
s	Seconds
SA	Social affect
SAD	Social anxiety disorder
SC	Superior colliculus
SCID-5-RV	Structured Clinical Interview for DSM-5 Disorders, Research Version
SCL-90	Symptom Checklist 90
SD	Standard deviation

SEC	Socio-Emotional Questionnaire
SLaM	South London and Maudsley
SMD	Standardised mean difference
SRS	Social Responsiveness Scale
SRS-2	Social Responsiveness Scale, Second Edition
SSRI(s)	Selective serotonin reuptake inhibitor(s)
STAI	State-Trait Anxiety Inventory
SWJ	Square wave jerk
TAS-20	Twenty-item Toronto Alexithymia Scale
TASIT	The Awareness of Social Inference Test
ToM	Theory of Mind
WASI-II	Wechsler Abbreviated Scale of Intelligence, Second Edition
WSAS	Work and Social Adjustment Scale

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Chapter 8

Dissemination of research

Publications included in the thesis

Kerr-Gaffney, J. E., Halls, D., Harrison, A., & Tchanturia, K. (2020). Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach. *Frontiers in Psychiatry, 11,* Article 401. https://doi.org/10.3389/fpsyt.2020.00401

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2019). Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis. *Frontiers in Psychiatry, 10,* Article 102. https://doi.org/10.3389/fpsyt.2019.00102

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2019). Eye-tracking research in eating disorders: A systematic review. *International Journal of Eating Disorders, 52,* 3-27. https://doi.org/10.1002/eat.22998

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa. *Journal of Affective Disorders, 266,* 273-281. https://doi.org/10.1016/j.jad.2020.01.169

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa. *European Eating Disorders Review, 28*(4), 433-444. https://doi.org/10.1002/erv.2736

Kerr-Gaffney, J. E., Mason, L., Jones, E., Hayward, H., Ahmad, J., Harrison, A., Loth, E., Murphy, D., & Tchanturia, K. (2020). Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits. *Journal of Clinical Medicine, 9*(4), Article 1057. https://doi.org/10.3390/jcm9041057

Publications completed during PhD but not included in the thesis

Cury, M. E., Berberian, A. A., Scarpato, B. S., **Kerr-Gaffney, J. E.**, Santos, F. H., & Claudino, A. (2020). Scrutinizing domains of executive function in binge eating disorder: A systematic review and meta-analysis. *Frontiers in Psychiatry, 11,* Article 288. https://doi.org/10.3389/fpsyt.2020.00288

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2018). Social anxiety in the eating disorders: A systematic review and meta-analysis*. Psychological Medicine, 48*(15), 2477-2491. https://doi.org/10.1017/S0033291718000752

Sedgewick, F., **Kerr-Gaffney, J. E.**, Leppanen, J., & Tchanturia, K. (2019). Anorexia nervosa, autism, and the ADOS: How appropriate is the new algorithm in identifying cases? *Frontiers in Psychiatry, 10*, Article 507. https://doi.org/10.3389/fpsyt.2019.00507

Manuscripts currently under review

Kerr-Gaffney, J. E., Mason, L., Jones, E., Hayward, H., Harrison, A., Murphy, D., Tchanturia, K. (2020). Autistic traits mediate reductions in social attention in adults with anorexia nervosa. Manuscript submitted for publication.

Lang, K., **Kerr-Gaffney, J**. **E.**, Hodsoll, J., Jassi, A., Tchanturia, K., & Krebs, G. (2019). Is poor global processing a transdiagnostic feature of Body Dysmorphic Disorder and Anorexia Nervosa? A meta-analysis. Manuscript submitted for publication.

Conference presentations associated with the thesis

Kerr-Gaffney, J. E. (2019, March). *Cognitive and affective empathy in anorexia nervosa* [Poster presentation]. International Conference on Eating Disorders, New York City, NY.

Kerr-Gaffney, J. E. (2019, April). *Social cognition and comorbid autism spectrum disorder traits in anorexia nervosa* [Paper presentation]. Cognitive Remediation for Anorexia Nervosa Conference, London, UK.

Kerr-Gaffney, J. E. (2020, March). *Exploring social anxiety symptoms in acute and recovered anorexia nervosa* [Paper presentation]. Eating Disorders International Conference, Glasgow, UK. (Conference cancelled)

Statement of work

Chapter 1: Introduction

This chapter is the candidate's own work. The candidate received minimal feedback and comments from her supervisors, Dr Amy Harrison and Prof Kate Tchanturia. Likewise, the published review included in the chapter is the candidates own work, shaped by comments from her supervisors. Dr Amy Harrison also replicated the search carried out in the review for reliability.

Chapter 2: Methods

This chapter is the candidate's own work. The candidate received minimal feedback and comments from her supervisors, Dr Amy Harrison and Prof Kate Tchanturia.

Chapter 3: The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa

The candidate collected and analysed the data, and wrote the manuscript presented in this chapter. The candidate's supervisors provided their comments on the manuscript, which were addressed prior to publication.

Chapter 4: Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach

The candidate collected and analysed the data, and wrote the manuscript presented in this chapter. The second author, Daniel Halls, provided guidance regarding methodology and contributed to data analysis. All co-authors provided comments on the manuscript, which were addressed prior to publication.

Chapter 5: Self-reported autistic traits mediate reductions in social attention in adults with anorexia nervosa

The candidate collected and analysed the data, and wrote the chapter. Dr Luke Mason and Prof Emily Jones performed data cleaning, and additionally Prof Emily Jones provided guidance regarding analyses. Hannah Hayward and Prof Declan

Murphy provided resources and guidance to enable the study to take place. Prof Kate Tchanturia read and provided minimal comments on the chapter.

Chapter 6: Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits

The candidate collected and analysed the data, and wrote the manuscript included in this chapter. Dr Luke Mason and Prof Emily Jones performed data cleaning, and additionally Prof Emily Jones provided guidance regarding analyses. Dr Jumana Ahmad and Dr Eva Loth developed and adapted the experimental paradigm. Hannah Hayward and Prof Declan Murphy provided resources and guidance to enable the study to take place. All co-authors read and provided comments on the manuscript.

Chapter 7: Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis

The candidate carried out the search, data extraction, analyses, and wrote the manuscript included in this chapter. The candidate's supervisors, Dr Amy Harrison and Prof Kate Tchanturia, provided comments on the manuscript which were addressed prior to publication.

Chapter 8: Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa

The candidate collected and analysed the data, and wrote the manuscript included in this chapter. The candidate's supervisors, Dr Amy Harrison and Prof Kate Tchanturia, provided comments on the manuscript which were addressed prior to publication.

Chapter 9: Discussion

This chapter is the candidate's own work. Prof Kate Tchanturia provided minimal comments on the chapter.

Structure of the thesis

This thesis incorporates publications. Figure 1 provides a map of the structure of the thesis.

Chapter 1 provides an overview of anorexia nervosa (AN) and common psychiatric comorbidities, including autism spectrum disorder (ASD). This introduction chapter also discusses interpersonal difficulties and socio-emotional cognition in individuals with AN, with a focus on empathy, perception of nonverbal communication, and social attention. A published review is included:

> Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2019). Eye-tracking research in eating disorders: A systematic review. *International Journal of Eating Disorders, 52,* 3-27. https://doi.org/10.1002/eat.22998

Chapter 2 outlines the general methods used across studies.

Chapter 3 is an empirical study examining ASD symptoms in individuals with AN, recovered AN, and healthy controls (HCs) using both self-report and clinical interview assessments:

> Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa. *European Eating Disorders Review, 28*(4), 433-444. https://doi.org/10.1002/erv.2736

Chapter 4 is an empirical study employing network analysis to map connectivity of ASD and eating disorder (ED) symptoms in individuals with AN:

> Kerr-Gaffney, J. E., Halls, D., Harrison, A., & Tchanturia, K. (2020). Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach. *Frontiers in Psychiatry, 11,* Article 401. https://doi.org/10.3389/fpsyt.2020.00401

Chapters 5 and 6 present empirical data on socio-emotional cognition in individuals with AN, one of which is a published paper:

> Kerr-Gaffney, J. E., Mason, L., Jones, E., Hayward, H., Ahmad, J., Harrison, A., Loth, E., Murphy, D., & Tchanturia, K. (2020). Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits. *Journal of Clinical Medicine, 9*(4), Article 1057. https://doi.org/10.3390/jcm9041057

Chapter 7 is a published review and meta-analysis of cognitive and affective empathic abilities in individuals with EDs:

> Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2019). Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis. *Frontiers in Psychiatry, 10,* Article 102. https://doi.org/10.3389/fpsyt.2019.00102

Chapters 8 is a published paper presenting empirical data on socio-emotional cognition in individuals with AN:

> Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa. *Journal of Affective Disorders, 266,* 273-281. https://doi.org/10.1016/j.jad.2020.01.169

Chapter 9 provides a general discussion of key findings, strengths and limitations of the current work, clinical implications, and concluding remarks.

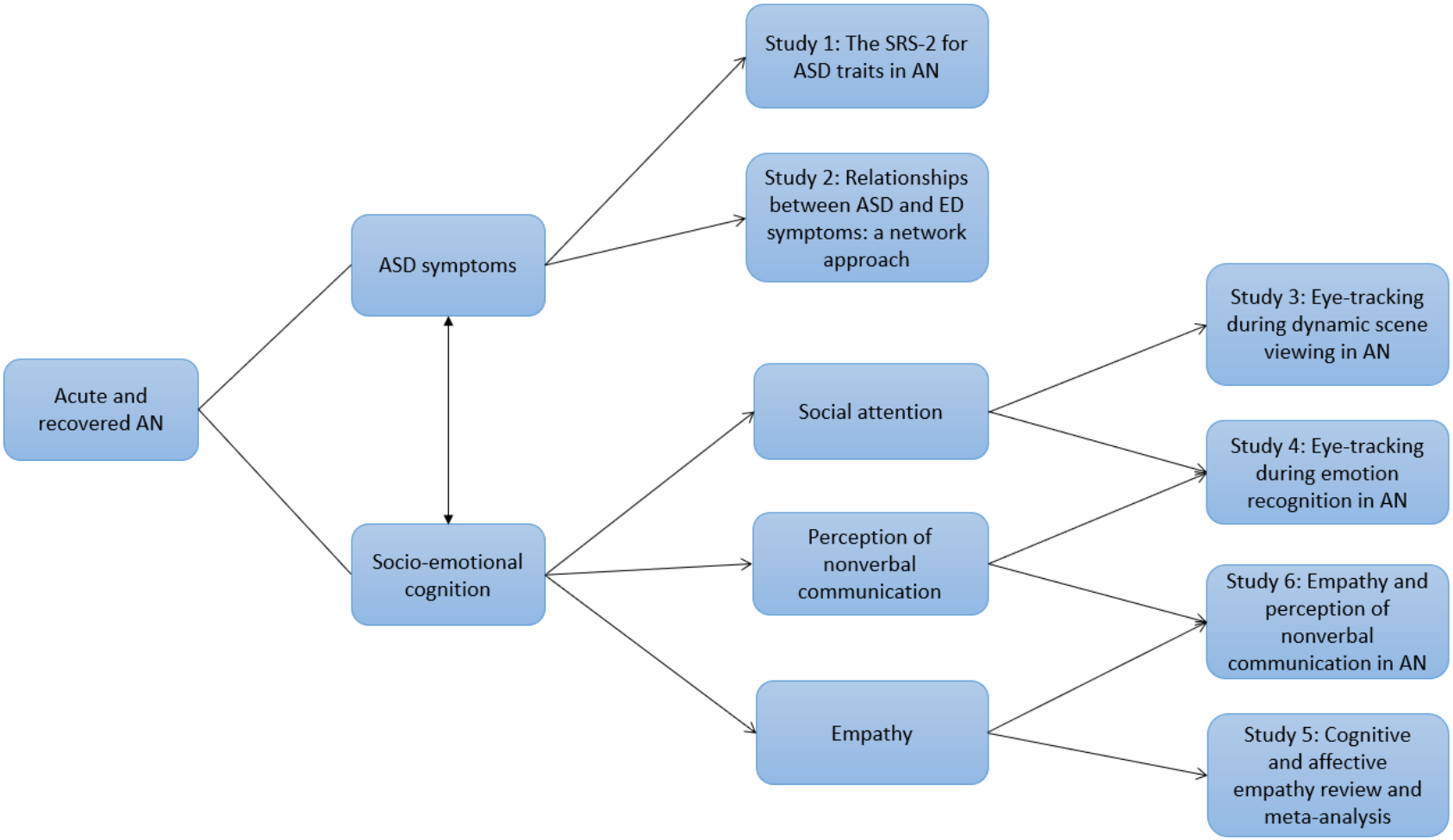

Figure 1. Thesis map

Chapter 1 - Introduction

1.1 Feeding and eating disorders

Feeding and eating disorders (EDs) are psychiatric disorders characterised by persistent disturbances in eating or eating-related behaviour, resulting in significant impairment in physical health or psychosocial functioning (American Psychological Association [APA], 2013). EDs are among the most common chronic illnesses in adolescents and are associated with high personal, familial, and economic costs (Gonzalez et al., 2007). For example, the annual economic cost of EDs in the United Kingdom (UK) is estimated to be around £15 billion when treatment costs, loss of earnings, and direct financial burdens to carers and sufferers are considered (Beat, 2015).

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2013) provides diagnostic criteria for anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED), avoidant/restrictive food intake disorder, pica, and rumination disorder. There is also a category for other specified feeding or eating disorder (OSFED), which applies to ED presentations that cause significant functional impairment, but do not meet full criteria for any of the aforementioned disorders. OSFED includes presentations such as atypical AN (where all criteria for AN are met, however weight is above or within the normal range) and purging disorder (frequent use of purging behaviour to influence weight or shape without binge eating).

1.2 Anorexia nervosa

AN is characterised by an intense fear of gaining weight, persistent behaviour to restrict energy intake (even when underweight), and a disturbance in the way one's body weight or shape is experienced (APA, 2013). The DSM-5 diagnostic criteria are as follows:

A. Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than

minimally normal or, for children and adolescents, less than that minimally expected.

B. Intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at a significantly low weight.
C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Specify whether:

Restricting type (AN-R): During the last three months, the individual has not engaged in recurrent episodes of binge eating or purging behaviour (i.e., self-induced vomiting or use of laxatives, diuretics, or enemas). Weight loss is accomplished primarily through dieting, fasting, and/or excessive exercise.

Binge-eating/purging type (AN-BP): During the last three months, the individual has engaged in recurrent episodes of binge eating or purging behaviour

1.2.1 Epidemiology and clinical course

AN is more common in females, with lifetime prevalence estimates ranging from <1 - 4% in this group (Keski-Rahkonen & Mustelin, 2016; Lindvall Dahlgren et al., 2017). The ratio of lifetime prevalence in males versus females is often reported as 1 : 10 (Hoek, 2006), however epidemiological studies, which may be less affected by clinical under-detection in males, have reported ratios as low as 1 : 3 (Hudson et al., 2007). Peak age of onset of AN is 15 to 19 years, with around 40% of cases occurring during this time (Herpertz-Dahlmann et al., 2015). However, time trend analyses suggest that age of onset is decreasing in younger generations (Favaro et al., 2009).

AN is a chronic and potentially life-threatening psychiatric disorder. Around half of individuals recover, 5% die from the illness, and 20% develop a chronic course of the disorder (Steinhausen, 2009). Indeed, AN is associated with one of the highest mortality rates of all psychiatric disorders, similar to that of substance use disorders (Arcelus et al., 2011; Chesney et al., 2014; Harris & Barraclough, 1998). Suicide is a

major cause of death in AN (Pompili et al., 2004), however at least one third of deaths in patients with AN are due to cardiac complications (Jáuregui-garrido & Jáuregui-lobera, 2012). Significant health issues in those with AN are common and include osteopenia, amenorrhea, growth retardation, cardiac arrhythmia, and changes in thyroid function (Katzman, 2005; Mehler & Krantz, 2003).

1.2.2 Treatment

International guidelines emphasise a multidisciplinary approach to treatment in AN, addressing psychological, medical, and nutritional needs. While outpatient care is recommended for most patients in the UK, inpatient care is considered when an individual's health is severely compromised, or when outpatient treatment has been ineffective (National Institute for Health [NICE], 2017).

Refeeding and nutritional rehabilitation is a necessary component of treatment for AN, however no single psychological intervention has proved to be particularly effective in treating the disorder (Fitzpatrick & Lock, 2009). In adolescents with AN, family-based treatment has been established as having a higher evidence grade compared to other treatments (NICE, 2017). For adults, NICE guidelines recommend either eating disorder-focused cognitive behavioural therapy, Maudsley anorexia nervosa treatment for adults, or specialist supportive clinical management. While there is some evidence to suggest these treatments demonstrate some improvements in key outcomes such as body mass index (BMI) and ED symptoms, one modality has not been shown to be consistently better than the others (Galsworthy-Francis & Allan, 2014; Schmidt et al., 2016). Further, recovery rates are low, with only around 30% of patients reaching full recovery at 1 or 2 year follow-up (Byrne et al., 2017; Schmidt et al., 2016). Some have argued that a plateau in AN treatment research has been reached, and that advances will depend on identification and treatment of core mechanisms underpinning AN psychopathology (Murray et al., 2019).

Similarly, although medications such as selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics are often used in patients with AN, evidence

regarding the efficacy of these pharmacological treatments is poor (Miniati et al., 2016). There are a few studies demonstrating improvements in depressive symptoms with fluoxetine treatment (Gwirtsman et al., 1990; Kim, 2003), and olanzapine has been shown to improve weight gain compared to placebo (Attia et al., 2019; Bissada et al., 2008). However, there are relatively few randomised controlled trials (RCTs) and studies are often underpowered due to limited sample sizes and high attrition rates.

Despite these rather disappointing findings, there is emerging evidence to suggest early intervention is an important factor in predicting good treatment outcomes in individuals with AN. Those with a shorter illness duration are more likely to recover, highlighting the importance of early intervention (Steinhausen, 2009; Treasure et al., 2015). This is thought to be due to the long term consequences of starvation and stress on the brain, causing ED behaviours and cognitions to become habitual over time (Treasure & Russell, 2011).

1.2.3 Maintenance models of AN

Several models have attempted to explain the persistence of AN, implicating biological, social, and psychological factors. It has been suggested that maintenance models are more likely to lead to treatment advances than aetiological accounts, since it is the maintenance mechanisms that need to be reversed if interventions are to be effective (Shafran & de Silva, 2003). A few relevant models are discussed here.

1.2.3.1 Cognitive-interpersonal maintenance model (Schmidt & Treasure, 2006; Treasure & Schmidt, 2013)

The cognitive-interpersonal maintenance model proposes that predisposing traits increase vulnerability to the development of AN, and also contribute to the maintenance of the disorder by strengthening pro-anorectic beliefs and behaviours. The model also proposes that AN is maintained interpersonally by both positive and negative reactions of close others in response to the illness. Two groups of predisposing traits are outlined by the model; obsessive-compulsive traits and anxious, avoidant, socio-emotional traits. It is proposed that increased attention to

detail and sensitivity to order (obsessive-compulsive traits) are predisposing factors. Once dieting is triggered (often by some precipitating factor, such as a stressful life event), it is undertaken meticulously and in a highly rigid manner. The resulting lack of nutrition reduces central coherence and global integration, further narrowing the focus on food and weight. Dieting becomes habitual, and a viscous cycle ensues. Indeed, empirical evidence shows that individuals with AN show weak central coherence, increased attention to detail, and set-shifting difficulties during the illness (Lang et al., 2014; Roberts et al., 2013; Tchanturia, Davies, Roberts, et al., 2012; Westwood et al., 2016) and after recovery (Danner et al., 2012; Fuglset, 2019; Tchanturia et al., 2004). There is also evidence to suggest difficulties in these domains are present in first degree relatives of individuals with AN (Holliday et al., 2005; Tenconi et al., 2010).

In the socio-emotional domain, sensitivity to stress and negative emotions, anxious and avoidant attachment styles, shyness, and negative self-evaluations are proposed to be predisposing factors for AN. Starvation reduces higher-level brain functioning, resulting in lowered social-processing abilities. This leads to further social withdrawal, allowing ED thoughts and behaviours to dominate. Furthermore, the presence of these traits in family members may contribute to further difficulties in communication and increase anxiety (Treasure et al., 2008). Correspondingly, empirical evidence has shown that individuals with AN show a variety of social difficulties both before and during the illness, including social anxiety, less social support, and fewer friendships (Arkell & Robinson, 2008; Gillberg et al., 1994; Hinrichsen et al., 2003; Krug et al., 2012; Schmelkin et al., 2017; Tiller et al., 1997). They also show difficulties in interpreting the emotions of others and expressing their own emotions (Caglar-Nazali et al., 2014). Thus, both predisposing factors and secondary consequences of the illness are involved in the maintenance of AN.

1.2.3.2 Transdiagnostic cognitive-behavioural model (Fairburn et al., 2003)

Originally developed to understand maintenance factors in individuals with BN, the cognitive-behavioural model was expanded to explain the persistence of other EDs, including AN. The model proposes that central to the maintenance of EDs is a

dysfunctional system of self-evaluation. While people without EDs evaluate themselves based on their perceived performance in a range of life domains (e.g., work, relationships, hobbies), those with EDs are thought to judge themselves mainly based on their eating habits, shape, and/or weight. Thus, control over one's diet and weight becomes one of the most important aspects of one's life.

In addition to this central psychopathology proposed to underlie EDs, four additional maintenance mechanisms are described. Firstly, clinical perfectionism in some individuals results in perfectionistic standards being applied to diet and weight (Bardone-Cone et al., 2007). This manifests as a fear of failure (e.g., weight gain, overeating), frequent and selective attention to performance (e.g., repeated calorie counting, body checking), and negatively biased appraisals of performance in these areas. The resulting negative self-evaluation promotes further striving to meet goals, maintaining the disorder (Shafran et al., 2002). Secondly, it is proposed that a proportion of individuals with EDs have core low self-esteem; a pervasive negative view of themselves which is part of their identity (Raykos et al., 2017). This maintains the ED as the individual pursues diet- and weight-related achievements to increase feelings of self-worth. Thirdly, mood intolerance results in some individuals using dysfunctional mood modulatory behaviours (e.g., binge eating, purging, intense exercise, self-harm) to cope with certain emotions (Cooper et al., 2004). This reduces awareness of the emotion and associated cognitions, and reinforces the belief that the ED can help deal with difficult emotions. Finally, interpersonal processes can contribute to the maintenance of EDs. For example, negative interpersonal events often precede ED behaviour, and long-term difficulties in relationships can undermine self-esteem (Murphy et al., 2012; Rieger et al., 2010).

The transdiagnostic theory suggests that while these mechanisms may differ at the individual level (i.e., not all four mechanisms are present in all individuals with EDs), they do not differ at the diagnostic level. That is, all four factors must be relevant across ED diagnoses. However, studies using structural equation modelling in transdiagnostic ED samples have only provided partial support for the model, suggesting that not all of the maintenance factors are equally related to core ED psychopathology across diagnoses (Lampard et al., 2013; Tasca et al., 2011).

1.2.3.3 Neurobiological model of the persistence of AN (Steinglass & Walsh, 2016)

The neurobiological model of AN proposes that persistent, maladaptive food restriction is the central behaviour maintaining the disorder. Laboratory studies show that restricted calorie and fat intake, as well as limited food range persist in AN even after recovery (Hadigan et al., 2000; Mayer et al., 2012; Sysko et al., 2005), and these restrictions are related to poor outcomes (Schebendach et al., 2008, 2012). The model takes a "top-down" approach to understand the underlying neurobiology related to this central maintenance factor in AN.

Abnormalities in brain areas associated with reward processing and habitual behaviour are implicated in the maintenance of AN. Differences in the mesolimbic reward system are consistently reported in individuals with AN, including the orbitofrontal cortex (OFC) and the nucleus accumbens (NAcc) (Cowdrey et al., 2011; Fladung et al., 2010; Frank et al., 2012, 2013; Titova et al., 2013). A range of disturbances are also reported in the frontostriatal systems, areas which are implicated in habitual behaviour (Delvenne et al., 1996, 1999; Titova et al., 2013; Wagner et al., 2007). When a behaviour changes from goal-directed to habitual (that is, it is repeated frequently until it is no longer dependant on receipt of a reward), there is a shift in the neural systems supporting the behaviour to the dorsal striatum and dorsolateral frontal cortex. Thus, persistent food restriction in AN is at first learned through reinforcement and is initially rewarding. As the behaviour becomes habitual, it becomes stereotyped and extremely difficult to alter, a process which is mediated by functioning in the dorsal frontostriatal systems (Foerde et al., 2015).

1.3 Comorbidity

Comorbidity in psychiatry is the rule rather than the exception; community epidemiological data suggests that of those with a psychiatric disorder, 45% meet diagnostic criteria for two or more diagnoses (Kessler et al., 2005). In treatment seeking groups, rates of comorbidity are often higher; up to 70-90% (Brown et al., 2001; Cancino et al., 2018; Simonoff et al., 2008). Further, comorbidity is strongly linked to severity; those with more diagnoses are more likely to be classified as having

severe difficulties (based on suicide attempts and functional impairment) compared to those with one diagnosis (Kessler et al., 2005). There is also evidence to suggest that the presence of comorbidities may moderate treatment response in a range of psychiatric disorders (Abramowitz, 2004; Berona et al., 2018; El-Mallakh & Hollifield, 2008; Steketee et al., 2001). Understanding the nature of these comorbidities may help inform and enhance future treatments.

Several theories regarding the underlying structure of psychopathology have attempted to explain the high rates of comorbidity between psychiatric disorders. For example, the general psychopathology (*p factor*) theory proposes that there is an underlying factor that accounts for the variance in symptoms across all forms of psychopathology (Caspi et al., 2014). Using confirmatory factor analysis, it has been demonstrated that adding the p factor improves the fit of structural models that organise symptoms associated with internalising and externalising disorders (Caspi et al., 2014). Higher scores on this general factor indicate increased risk of developing a psychiatric disorder, and also correlate strongly with personality, life impairment, developmental history and brain integrity (Laceulle et al., 2015). The general factor likely has a genetic component; genes involved in the development of psychopathology tend to enhance risk for all disorders rather than specific ones (Lahey et al., 2011; Selzam et al., 2018).

On the other hand, the network analysis approach to psychopathology proposes that psychiatric disorders are constellations of symptoms, which activate one another (Borsboom, 2017). The relationships between symptoms are key to the development and maintenance of psychopathology; symptoms can form feedback loops, eventually producing a set of symptoms that are recognised as a psychiatric disorder. Symptoms in one cluster can activate symptoms in other clusters, and such symptoms are termed *bridge nodes*. For example, excessive worry – a symptom in the general anxiety disorder diagnostic cluster - might activate fear of weight gain in the ED diagnostic cluster (Forrest et al., 2019). Thus, having symptoms of one disorder puts an individual at risk of developing other disorders. Bridge symptoms may be important targets in treating or preventing comorbidity (Jones et al., 2019).

1.3.1 Depressive disorders

Depressive disorders share common features of sad, empty, or irritable mood, as well as somatic and cognitive changes. Major depressive disorder (MDD) is the most common of these disorders, and is characterised by a depressive episode lasting for at least two weeks, during which there is either depressed mood or loss of interest in usual activities (APA, 2013). In addition, symptoms such as changes in appetite, weight, or sleep, decreased energy, difficulty thinking and concentrating, and feelings of worthlessness or guilt are also present. MDD is associated with significant distress and impairment in functioning, and is one of the leading causes of disability worldwide (World Health Organisation, 2017). Lifetime prevalence is around 16.2%, and MDD is diagnosed in women at a rate 1.5 to three times higher than in men (Kessler et al., 2003). MDD is highly comorbid with other health conditions; with around 60-70% of patients having at least one comorbid psychiatric disorder, and two thirds having at least one physical health condition (Otte, 2008). Psychiatric comorbidity is a predictor of poor outcome in individuals with MDD (Novick et al., 2017; Viinamäki et al., 2006).

1.3.1.1 Rates of depression in AN

MDD is one of the most common comorbid psychiatric disorders in people with AN, with a lifetime prevalence of around 50-75% (Calugi et al., 2014; Fernandez-Aranda et al., 2007; Godart et al., 2007). There is some evidence to suggest that MDD is more common in those with AN-BP compared to those with AN-R (Giovanni et al., 2011; Fernandez-Aranda et al., 2007). Rates of persistent depressive disorder (formerly dysthymia) are also elevated in individuals with AN, although lifetime prevalence estimates are more varied (8-92.9% compared to 0.9% in the general population) (Blanco et al., 2010; Godart et al., 2007). In addition to those who meet diagnostic criteria for a depressive disorder, a considerable proportion of individuals with AN also show clinically significant depressive symptomatology on self-report questionnaires, but do not necessarily meet full criteria for a depressive disorder diagnosis (Giovanni et al., 2011; Miniati et al., 2018). High levels of depression are associated with more severe ED psychopathology (Boehm et al., 2018; Giovanni et

al., 2011), suicide attempts (Ahn et al., 2019), relapse (Kahn et al., 2019) and poorer outcomes in AN (Franko et al., 2018; Smith et al., 1993; Vall & Wade, 2015). In addition, recent studies using network analysis have demonstrated the importance of comorbid depression alongside core ED psychopathology in maintaining AN (Monteleone et al., 2019; Solmi et al., 2019).

1.3.1.2 Depression comorbidity: state or trait effects?

Several explanations for the relationship between AN and depression have been offered (Casper, 1998). Firstly, depression may be a predisposing factor for AN. For example, symptoms of depression such as loss of appetite or low self-esteem may activate an underlying vulnerability for AN. Alternatively, the effects of the ill state, such as starvation or low body weight, may produce depression-like symptoms in individuals with AN, which would be expected to ameliorate with recovery. Thirdly, both disorders might arise from a common aetiology.

Studies documenting the effects of starvation or calorie restriction in healthy volunteers have provided some insight into the nature of the relationship between depression and AN. In the Minnesota Starvation Experiment, healthy men were placed on a 24 week starvation diet in order to examine the impact of various nutritional rehabilitation strategies for the post-World War II aid effort (Keys et al., 1950). The men lost on average 25% of their body weight, and experienced periods of severe emotional distress and depression during the study. Mood changes lasted 6-12 months post-nutritional rehabilitation. Interestingly, using the same questionnaire to assess psychological and physical symptoms as in the Minnesota Starvation Experiment, Hagan et al. (2000) reported that self-reported dietary restraint was associated with increased depression, irritability, and apprehension in university students. Laessle et al. (1996) found that alternating a diet of restriction with unlimited eating for four weeks was associated with increased irritability, lowered mood, increased fatigue, and difficulties concentrating in healthy women. Thus, restricting food intake can produce symptoms associated with depression in healthy individuals. It is therefore possible that depression in those with AN is a product of starvation. However, it is not known whether the mood changes seen in

the dietary restriction studies reached clinical levels, as is seen in AN, as diagnostic instruments for depressive disorders were not used.

Similarly, studies have assessed depression in individuals who have recovered from AN in order to examine potential relationships with clinical state. The evidence from cross-sectional studies is mixed, with some reporting lower levels of depression in those recovered from AN compared to individuals in the acute stage (Harrison et al., 2014; Oldershaw et al., 2010), and others reporting higher levels of depression in recovered and acute AN relative to HC (Harrison, Tchanturia, & Treasure, 2010; Morris et al., 2014). This is likely a result of differing inclusion criteria (for example, whether HC participants were included on the basis of absence of ED symptoms or wider psychopathology) and depression measures used. A few longitudinal studies have also measured depressive symptoms following weight restoration in AN. For example, Pollice et al. (1997) found that levels of depression did not significantly change in individuals with AN admitted to inpatient treatment after short-term weight restoration (to at least 90% average body weight). Scores in this group were significantly higher than those of a long-term recovered group and HCs, who did not differ from one another. A study by Boehm et al. (2018) used similar methodology, finding that there was a significant reduction in depression scores after short-term weight restoration in inpatients with AN. Similar to the previous study, levels of depression were significantly higher in the short-term weight restored group compared to a long-term recovered group and HCs, who did not differ from one another.

From these studies, it could be concluded that the high levels of depression seen in AN are associated with the ill state, and return back to normal levels after long-term recovery. However, long-term recovery was not assessed longitudinally in these studies, instead a separate group of recovered participants were compared to the current AN/short-term weight restored group. To overcome this limitation, Holtkamp et al. (2005) examined a group of former inpatients with AN at discharge from hospital, and at 3, 7, and 10 years post-discharge. Participants were required to be recovered for at least 3 years at the 10 year follow-up to be included in the study. Depression scores did not differ between discharge and 3 year follow-up, but

significantly decreased between 3 and 7 year follow-up. There was no change between 7 and 10 year follow-up, where scores remained elevated compared to a HC group. Thus, while some of the depressive symptoms seen in AN may be due to starvation effects, this does not appear to be the only explanation for the high levels of comorbidity.

Studies documenting the chronology of appearance of MDD and AN have perhaps been most informative in understanding the nature of the relationship between the two disorders. These studies have reported that in around 25 to 50% of cases, MDD preceded onset of AN by at least 1 year (Carrot et al., 2017; Fernandez-Aranda et al., 2007; Smith et al., 1993). In addition, a few studies have demonstrated the predictive effects of premorbid depressive symptoms on ED psychopathology. Keski-Rahkonen et al. (2014) identified a group of women with AN from a nationwide cohort at age 16, and followed them up at age 22-28 years. At follow-up, 71% had recovered from AN, and this group were less likely to have suffered from MDD prior to AN onset (2.6%) than those who had not recovered (18.8%). Other factors associated with decreased likelihood of recovery included unemployment, perfectionism, and a poor relationship with their current partner. However, when all prognostic factors were adjusted for age of onset, premorbid depression remained the only significant predictor of persisting AN.

These findings suggest that there are a few different explanations contributing to comorbidity between AN and depressive disorders. Keeping in mind the limitations of retrospective reporting, studies investigating chronology of onset rule out the possibility that depression is solely a result of starvation or low body weight in AN, although exacerbation of symptoms in the ill state is likely. It may be that some individuals have an underlying predisposition to developing both disorders, and their expression might be triggered by similar events, such as puberty or trauma (Fernandez-Aranda et al., 2007). Finally, cases where the onset of depression occurs before AN may represent a more persistent form of illness, which may require special consideration during treatment (Keski-Rahkonen et al., 2014).

1.3.2 Anxiety disorders

Anxiety disorders are the most common of all psychiatric disorders, with a lifetime prevalence of up to 33.7% in adults in the general population (Bandelow & Michaelis, 2015). They are characterised by excessive fear and anxiety and related behavioural disturbances, although the objects or situations that elicit symptoms differ across anxiety disorder subtypes (see Table 1). Among the most common anxiety disorders are specific phobia, social anxiety disorder (SAD), and generalised anxiety disorder (GAD). Generally, rates of anxiety disorders are twice as high in woman than men, and median age of onset is 11 years (Bandelow & Michaelis, 2015). Comorbidity both between anxiety disorders and with other psychiatric disorders such as depression is common.

Table 1. Key symptoms of common DSM-5 anxiety disorders

Specific Phobia	Persistent, marked fear/anxiety about a specific object or situation, out of proportion to actual danger or context.
Social Anxiety Disorder	Persistent, marked fear/anxiety about social situations, in which the individual fears they will act in a way or show anxiety symptoms that will be negatively evaluated by others.
Panic Disorder	Recurrent panic attacks, that are followed by persistent worry about future attacks and/or a maladaptive change in behaviour.
Agoraphobia	Persistent, marked fear/anxiety about situations where escape might be difficult or help may not be available (e.g., public transport, being in open or enclosed spaces).
General Anxiety Disorder	Excessive anxiety/worry about a variety of events/activities, that occur most of the time and are difficult to control. Accompanied by somatic symptoms such as restlessness, fatigue, and sleep disturbances.

1.3.2.1 Rates of anxiety disorders in AN

Lifetime prevalence estimates of any anxiety disorder in those with AN range from 23% to 83% (Swinbourne & Touyz, 2007). However, most estimates include obsessive

compulsive disorder (OCD) and post-traumatic stress disorder, which are no longer included as anxiety disorders in the DSM-5. More recently, Udo & Grilo (2019) reported a lifetime anxiety disorder prevalence of 40.5% in individuals with AN from a large nationally representative sample. Most studies report SAD as the most common comorbid anxiety disorder in those with AN, with lifetime prevalence estimates ranging from 16 to 55% (Swinbourne & Touyz, 2007). However, GAD and specific phobias are also common (Kaye et al., 2004; Tchanturia, Davies, Harrison, et al., 2012). In addition to categorical prevalence estimates, individuals with AN consistently show higher scores on self-report measures of anxiety relative to HCs (Dapelo et al., 2016; Harrison et al., 2010, 2014; Schneier et al., 2016; Steinglass et al., 2017). In fact, scores are sometimes as high as those reported in anxiety disorder samples (Bulik et al., 1991; Grabhorn et al., 2006; Hartmann et al., 2019).

1.3.2.2 Associations between anxiety and AN symptoms

Several lines of evidence suggest that anxiety has a functional impact upon AN symptomatology. As well as self-reported anxiety being associated with more severe ED symptoms in AN (Goddard & Treasure, 2013; Haynos et al., 2015; Peñas-Lledó et al., 2002), the presence of a premorbid anxiety disorder is associated with more severe ED symptoms and lower quality of life (Carrot et al., 2017; Dellava et al., 2010; Raney et al., 2008). Secondly, anxiety may be an important prognostic factor; higher trait anxiety predicts lower likelihood of recovery in those with AN (Yackobovitch-Gavan et al., 2009; Zerwas et al., 2013). It is proposed that those with higher anxiety may find it more difficult to relinquish AN behaviours – such as food restriction or exercise – which serve to reduce anxiety (Dellava et al., 2010). Finally, momentary variations in anxiety are temporally related to ED behaviours in those with AN (Lavender et al., 2013). In the moments leading up to ED behaviours there is an increase in anxiety, and in the moments after the behaviour, anxiety declines (Hartmann et al., 2019). In this way, reductions in anxiety may negatively reinforce ED behaviours.

Using network analysis, a few studies have examined which ED symptoms in individuals with AN or BN might explain anxiety comorbidity. Forrest et al. (2019)

found that the ED symptom with the strongest association to trait anxiety was avoidance of social eating, while the trait anxiety node with the strongest association to the ED cluster was low self-confidence. A similar finding was reported in a network analysis of SAD and ED symptoms, where fears around eating and drinking in public were the strongest bridge symptoms between diagnostic clusters (Levinson et al., 2018). Thus, fears and avoidance of eating and drinking in public may be routes through which anxiety disorders and EDs can co-occur. Avoidance of eating around others may reduce anxiety in the short-term, negatively reinforcing the ED behaviour and increasing the likelihood of avoidance next time.

1.3.2.3 Anxiety comorbidity: state or trait effects?

Similar to depressive symptoms, it has been suggested that anxiety symptoms in AN are sequelae of malnutrition (Mattar et al., 2011). However, several studies have reported that general anxiety and social anxiety symptoms are not associated with BMI in individuals with AN (Mattar et al., 2011; Mattar, Huas, et al., 2012; Mattar, Thiébaud, et al., 2012), suggesting elevated anxiety may not be a result of the ill state. Cross-sectional studies have provided mixed evidence as to whether anxiety remains elevated in individuals who have recovered from AN. Some have shown that recovered individuals exhibit intermediate levels of anxiety, significantly higher than that of HCs but lower than individuals in the acute stage of illness (Dapelo et al., 2016; Leppanen, Dapelo, et al., 2017). A similar finding has been reported regarding levels of social anxiety (Schmelkin et al., 2017). Others report no differences between recovered AN and HCs on self-report anxiety measures (Harrison et al., 2010; 2014). Very few studies have examined patterns of anxiety longitudinally past short-term weight restoration, however one study found that at 10 year follow-up, individuals in long-term recovery from AN (>3 years) still had significantly higher levels of anxiety relative to HCs (Holtkamp et al., 2005).

Studies examining chronology of onset have also given some insight into the nature of the relationship between anxiety disorders and AN. Several retrospective studies report that in most cases, anxiety disorders precede AN onset (Bulik et al., 1997; Carrot et al., 2017; Godart et al., 2000). However, results may differ across anxiety

disorders. For example, in those with SAD and AN, SAD was found to precede AN onset in around two thirds of cases, whereas in individuals with GAD and AN, GAD was found to precede AN onset in only 29-46.5% of cases (Carrot et al., 2017; Godart et al., 2000). However, this is likely due in part to the much later median age of onset of GAD (30 years, compared to 13 years in SAD) (Kessler et al., 2012). Individuals with AN also report higher childhood anxiety compared to HCs, supporting the notion that anxiety may be a predisposing factor for AN (Kim et al., 2010; Marzola et al., 2019). Few longitudinal studies have examined whether premorbid anxiety disorders increase risk of subsequent AN. Schaumberg et al. (2019) collected parental reports of anxiety symptoms in a large sample of children at age 10, finding that anxiety symptoms involving worry predicted diagnoses of AN at age 14 and disordered eating at age 16. Further, in a Danish population register study, OCD, SAD, and GAD were associated with a significantly increased risk of later AN, particularly in males with an anxiety disorder (Meier et al., 2015).

Thus, a small number of studies suggest anxiety disorders usually predate AN onset in those with both disorders. There is also some evidence to suggest that anxiety disorders may be risk factors for the development of AN. Indeed, it has been suggested that anxiety may represent a genetically mediated pathway for the development of AN, as evidenced by twin studies demonstrating shared transmission of anxiety disorders and EDs (Keel et al., 2005), and aggregation of anxiety disorders in first degree relatives of individuals with AN (Strober et al., 2007). Evidence regarding persistence of anxiety after recovery is inconsistent, and further longitudinal studies are required.

1.3.3 Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterised by deficits in social communication and interaction, and restrictive, repetitive patterns of behaviour or interests which cause significant impairments in functioning (APA, 2013). ASD affects around 1% of the population, is highly heritable, and symptoms are typically recognised during early childhood (Brugha et al., 2011). ASD is more commonly diagnosed in males than females, with a gender ratio of around 4 : 1 often

reported (Fombonne, 2009). However, the gender ratio varies considerably across studies; with ratios as low as 3 : 1 in studies that screen population-based samples (Loomes et al., 2017). Several factors have been proposed to contribute to under detection of ASD in females. For example, diagnostic tools have been impacted by the longstanding gender bias towards male presentations, resulting in a lack of sensitivity to female presentations (Adamou et al., 2018; Lai et al., 2015). Further, compared to males, females with ASD use more social coping strategies such as camouflaging in order to fit in (Lai et al., 2017). These techniques, which include the use of eye-contact, using learned phrases, or imitating others' facial expressions and body language, may lead to the symptoms of ASD going unnoticed by families and teachers in childhood, and even during diagnostic assessments (Lai et al., 2011).

1.3.3.1 Similarities in the phenotypic expressions of AN and ASD

A possible overlap between ASD and AN was first proposed by Gillberg (1983), who noted the obsessive insistence on sameness and problems with social relationships seen in both individuals with ASD and those with AN. Since then, empirical research has confirmed the similarities in phenotypic expressions of both disorders. For example, difficulties in set-shifting, an executive function involving the ability to move back and forth between tasks, rules, or operations, are seen in individuals with AN, and may underlie the rigid and restrictive behaviour towards food and weight characteristic of the disorder (Westwood et al., 2016). Interestingly, these difficulties do not seem to be a result of the ill state, persisting in those who are fully recovered from AN (Danner et al., 2012; Holliday et al., 2005; Lindner et al., 2014; Tchanturia, Davies, Roberts, et al., 2012). Further, healthy sisters of those with AN show poorer set-shifting abilities compared to HCs, suggesting that difficulties in this area may be heritable traits (Holliday et al., 2005; Roberts et al., 2010; Tenconi et al., 2010). Similarly, inefficiencies in set-shifting abilities are also apparent in individuals with ASD, of similar magnitude to those seen in AN (Westwood et al., 2016). Poor set-shifting abilities have also been demonstrated in parents of those with ASD compared to parents of HCs (Hughes et al., 1997; Wong et al., 2006), supporting the idea that set-shifting ability may be a trait marker for the disorder (Zhou et al., 2017).

Individuals with AN often display perfectionistic and detail-focussed thinking styles, finding it difficult to "see the bigger picture" (Lloyd et al., 2014). It is thought that this cognitive style may maintain the ED through an obsessive adherence to dietary rules and detail. Indeed, empirical work has shown that those with AN show better performance on neuropsychological tasks that require detailed, local processing, but perform poorly on tasks of central coherence (*global processing*) (Lang et al., 2014; Lang, Roberts, et al., 2016). Similar to set-shifting performance, superior detail processing is also seen in those recovered from AN, as well as unaffected sisters (Lopez et al., 2008; Roberts et al., 2013; Tenconi et al., 2010). Weak central coherence may also be linked to the restrictive and repetitive behaviours that characterise ASD. Similar to those with AN, individuals with ASD show superior local processing relative to HCs (Jolliffe & Baron-Cohen, 1997; Shah & Frith, 1993), alongside poorer global processing abilities (Happé & Booth, 2008). Parents of those with ASD also show a bias for local processing when compared to HCs (Baron-Cohen & Hammer, 1997; Bölte & Poustka, 2006; Happé et al., 2003), suggesting this processing style may be a heritable trait independent of the presence of the disorder itself.

Moving to the socio-emotional domain, there is evidence to suggest differences in theory of mind (ToM) abilities in individuals with AN. ToM is the ability to attribute mental states (intents, emotions, beliefs, etc.) to others, and understand that these may differ from one's own. Several studies have reported lower ToM performance in individuals with AN compared to HCs (Russell et al., 2009; Tapajõz Pereira De Sampaio et al., 2013), with more severe difficulties associated with a longer duration of illness (Bora & Kose, 2016). This finding might suggest ToM difficulties are related to the ill state, perhaps due to prolonged starvation. However, difficulties in this area have also been reported in those recovered from AN (Harrison, Tchanturia, & Treasure, 2010; Oldershaw et al., 2010), as well as unaffected twin siblings (Kanakam et al., 2013). The ToM account of ASD posits that impairments in ToM could explain many of the behavioural symptoms that characterise the disorder (Baron-Cohen et al., 1985). While the theory has now been expanded to include other cognitive mechanisms (including those discussed above) (Happé et al., 2006), impaired ToM performance has been replicated extensively in individuals with ASD (Peñuelas-Calvo

et al., 2019). Lower ToM abilities have also been reported in unaffected parents and siblings of individuals with ASD (Eyuboglu et al., 2018; Nagar Shimoni et al., 2012). A recent review concluded that individuals with ASD and AN show similar difficulties in ToM compared to HCs, however those with ASD show more difficulties in tasks that assess emotional ToM (Leppanen et al., 2018).

1.3.3.2 Rates of ASD in AN

As well as showing similarities in neuropsychological and socio-emotional profiles, those with AN display high levels of ASD traits. For example, individuals with AN show higher levels of ASD symptoms on self-report screening measures such as the Autism Quotient (AQ; Baron-Cohen et al., 2001), relative to HCs (Westwood, Eisler, et al., 2016). Studies using more robust assessments of ASD symptoms, such as the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2; Lord et al., 2012), have also found elevated rates of ASD symptoms in those with AN. The ADOS-2 is a standardised semi-structured interview recommended in the assessment of ASD (NICE, 2012), and provides a cut-off score to indicate whether symptoms are clinically significant. Using the ADOS-2, studies have reported that between 4 and 52.5% of individuals with AN meet the criteria for ASD (Postorino et al., 2017; Westwood et al., 2018).

The ADOS-2 is limited in that it only provides an assessment of current ASD symptoms. Given that ASD is a developmental disorder, symptoms must also be present in early childhood. Few studies have examined rates of ASD in AN using both a developmental interview and a clinical assessment of current symptoms. Westwood et al. (2018) found that although 52.5% of adolescents with AN scored above the clinical cut-off for ASD on the ADOS-2, only 10% also scored above cut-off on the Developmental, Dimensional and Diagnostic Interview, short version (3Di-sv; Santosh et al., 2009) and thus met full research criteria for ASD. Therefore, a significant proportion of individuals may not necessarily meet full criteria for a diagnosis of ASD, but nonetheless show high levels of ASD traits. Given that the presence of high ASD traits in AN is associated with poorer outcomes (Anckarsäter et al., 2012; Nielsen et al., 2015; Wentz et al., 2009), and less improvement during

treatment (Stewart et al., 2017; Tchanturia et al., 2016), using a dimensional approach to symptoms may nonetheless be useful.

1.3.3.3 ASD comorbidity: state or trait effects?

Individuals without EDs who are subject to starvation show certain characteristics of ASD, such as reduced social motivation and cognitive rigidity (Keys et al., 1950). It has therefore been suggested that high levels of ASD traits found in a proportion of those with AN may be due to the effects of starvation, and do not represent true ASD (Hiller & Pellicano, 2013). However, several studies have found that BMI, which is often used as a measure of illness severity, is not associated with ASD traits in individuals with AN (Bentz et al., 2017; Calderoni et al., 2015; Nazar et al., 2018; Sedgewick et al., 2019; Tchanturia et al., 2019; Vagni et al., 2016; Westwood, Mandy, et al., 2017a). A few of these studies also examined associations with illness duration, finding that those with high ASD traits had not been ill for a significantly longer period of time than those with low ASD traits (Nazar et al., 2018; Westwood, Mandy, & Tchanturia, 2017a). The association between ASD symptoms and ED psychopathology (measured using self-report questionnaires) is more mixed. While Tchanturia et al. (2019) found that ASD symptoms were positively associated with scores on the Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994) in a large group of inpatients with anorexia, others have found no such association (Bentz et al., 2017; Sedgewick et al., 2019; Westwood, Mandy, & Tchanturia, 2017a). The converging findings might be due to differences in the way ASD traits were measured; the former study used the Autism Quotient, abbreviated version (AQ-10), while the latter three studies used the ADOS-2. Thus, it appears that ASD symptoms are not associated with measures of acute illness severity, suggesting they are not a product of the ill state.

Given the lack of studies using developmental ASD assessments in AN, research in individuals recovered from the disorder can also give some insight as to whether ASD symptoms are independent of the ill state. Cross-sectional studies have found elevated levels of ASD traits in recovered individuals compared to HCs. For example, Bentz et al. (2017) found that a significantly higher proportion of both acute (16%) and recovered AN (21%) scored above the clinical cut-off on the ADOS-2 compared

to HCs (0%). Similarly, Sedgewick et al. (2019) found that a significantly higher proportion of individuals with acute (27.3%) and recovered AN (19.6%) scored above the ADOS-2 cut-off compared to HCs (9.5%). To date, one longitudinal study has examined the stability of ASD diagnoses in a representative community sample of individuals with AN. Fifty-one participants with adolescent-onset AN and a group of age- and sex-matched controls were examined at age 16 (baseline) (Gillberg & Råstam, 1992), age 21 (Gillberg et al., 1994), age 24 (Råstam et al., 2003), and age 32 (Anckarsäter et al., 2012; Wentz et al., 2009). The proportion of participants who had recovered at each time point varied between 39% and 54%. Summarising the results from the four waves of the study, Nielsen et al. (2015) reported that 32% of the AN group had at one or more assessments been given a diagnosis of ASD. However, only 12% met criteria at all four time points. Due to changes in diagnostic criteria for ASD and different diagnostic assessments being used across study time points, it is difficult to draw conclusions regarding the stability of the ASD diagnoses. In a further report including recovered individuals only at 30 year follow-up, 23% were reported to have received a diagnosis of ASD in at least three of the four assessments (Dinkler et al., 2019), a rather similar proportion to that reported in the aforementioned cross-sectional studies. Overall, it seems that ASD traits remain elevated in individuals recovered from AN, however methodological limitations prevent firm conclusions from being made.

1.4 Interpersonal functioning in AN

1.4.1 Interpersonal functioning and mental health

Interpersonal functioning, which describes our interactions and relationships with others, is key to good mental health. Attachment theory proposes that the way in which social interactions are internalised provides a base for psychological development, forming part of our self-image (Berkman & Glass, 2000; Waters & Waters, 2006). When asked what gives their lives meaning and happiness, most individuals report the importance of having secure and fulfilling relationships with others (Berscheid & Peplau, 1983; Klinger, 1977). Indeed, perceived social support has been consistently linked with positive affect (Finch et al., 1999; Waldinger et al.,

2015), lower psychological distress (Barrera, 1986; Cohen & Wills, 1985), and lower rates of depression (Cheng et al., 2014; Lakey & Cronin, 2008). Conversely, interpersonal difficulties and negative social experiences are associated with a range of psychiatric disorders, including anxiety and depression (Bertera, 2005; Petty et al., 2004), schizophrenia (Blanchard et al., 1998; Wallace, 1984), and EDs (Arcelus et al., 2013).

1.4.2 Interpersonal difficulties during the acute state of AN

Recent models of AN have put forward interpersonal difficulties as a key factor in the development and maintenance of the disorder (Arcelus et al., 2013; Cardi, Tchanturia, et al., 2018; Treasure & Schmidt, 2013). During the illness, a variety of social difficulties are seen. For example, individuals with AN report poorer social skills compared to HCs (Rhind et al., 2014), a finding that has been confirmed by parental reports (Bentz et al., 2017; Winecoff et al., 2015). Experimental work has shown that people with AN use fewer positive and more negative social problem-solving strategies relative to HCs (Oldershaw et al., 2015; Sternheim et al., 2012). In addition, research has documented reduced social networks, lower social support, and isolation during the illness (Adenzato et al., 2012; Arkell & Robinson, 2008; Gillberg et al., 1994; Tiller et al., 1997), as well as a shy and inhibited temperament in those with AN (Adambegan et al., 2012; Cardi, Tchanturia, et al., 2018; Winecoff et al., 2015). Individuals with AN also show high levels of social anhedonia (loss of interest and low motivation to engage in pleasurable social activities), a factor that is associated with a longer duration of illness and more work and social adjustment problems (Harrison et al., 2014; Tchanturia, Davies, Harrison, et al., 2012). Qualitative reports of individuals' own experiences have qualified these findings. For example, both adults and adolescents with AN report reduced social networks, isolation, and social communication difficulties, problems that are often exacerbated by long hospital stays (Doris et al., 2014; Patel et al., 2016; Westwood, Lawrence, et al., 2016).

1.4.3 Interpersonal difficulties before illness onset and after recovery

There is some evidence to suggest that interpersonal problems are apparent before illness onset. Up to two thirds of individuals with AN report having early social difficulties (Cardi, Mallorqui-Bague, et al., 2018; Gillberg & Råstam, 1992), and are more likely to report having no childhood friends compared to HCs (Fairburn et al., 1999). Individuals with AN are also more likely to have a history of being bullied compared to HCs (Lie et al., 2019), and display more internalising problems in childhood (Adambegan et al., 2012). Finally, a large multi-centre study found that those with AN engage in more solitary activities in childhood, a pattern that continues into adulthood (Krug et al., 2012). These findings suggest that problems in the social domain may be a trait phenomenon, although they may be exacerbated by starvation or other factors associated with the ill state. However, research in this area is limited in that the majority of studies use retrospective reporting, and thus may be subject to recall biases. Prospective research is difficult due to low base rates of AN among the general population.

Relatively few studies have examined social functioning in those recovered from AN. Generally, this research suggests that social difficulties often persist after recovery, albeit in an attenuated form. For example, Harrison et al. (2014) reported that levels of social anhedonia in those recovered from AN were significantly higher than those reported by HCs, but lower than those of an acute AN group. In the recovered group, 30% scored above the cut-off indicating clinically significant levels of social anhedonia, and these individuals reported significantly more work and social functioning difficulties than those with low social anhedonia scores. Similarly, poorer social skills have been reported in acute and weight-restored AN, relative to HCs (Winecoff et al., 2015). Individuals recovered from AN also show a tendency towards submissive behaviour and negative social comparison, with scores on self-report measures lying between that of acute AN and HCs (Cardi, Matteo, et al., 2014; Connan et al., 2007).

1.4.4 Interpersonal functioning as a prognostic factor

As well as being associated with more severe ED psychopathology (Illing et al., 2010; O'Mahony & Hollwey, 1995; Tasca et al., 2011), interpersonal difficulties are an important prognostic factor in AN. A systematic review including seven studies in AN showed that interpersonal problems at the start of treatment were associated with detrimental treatment outcomes across ED subtypes (Jones et al., 2015). The authors suggest this relationship could be mediated by the client-therapist relationship, such that interpersonal problems such as social avoidance make engaging in treatment difficult. Indeed, Hartmann et al. (2010) demonstrated that in individuals with AN-BP, social avoidance predicted smaller reductions in binge severity during treatment. In those with AN-R, interpersonal problems in the dominance domain were associated with less weight gain during treatment. Longitudinal studies with long follow-up periods have also demonstrated the importance of social functioning on recovery. For example, Deter et al. (2005) examined individuals with AN 12 years after an inpatient admission, finding that social pathology was one of the best predictors of poor outcome (Morgan-Russell scores; Morgan & Hayward, 1988). Wentz et al. (2009) found that problems with friendship before AN onset were predictive of outcome 18 years after diagnosis, and Zipfel et al. (2000) found that social problems predicted poor outcome 21 years after first inpatient treatment. In addition, Franko et al. (2013) reported that poor social adjustment was a significant predictor of mortality in women with AN at 20 year follow-up.

Qualitative studies have complimented these findings, consistently emphasising the importance of social support in recovery. In a review of studies examining former patients' and therapists' views on what constitutes recovery, social relations and participation was identified as a key theme by both groups (Noordenbos, 2011). Those recovered from AN and other EDs report that reconnecting with others and developing supportive relationships are key to recovery and decreasing isolation (Beresin et al., 1989; Cockell et al., 2004; Linville et al., 2012). Federici and Kaplan (2008) interviewed participants with AN 14 months after discharge from inpatient or intensive outpatient treatment, comparing those who remained weight restored to

those who subsequently relapsed. Developing supportive relationships was identified as a key theme; recovered participants emphasised the importance of the support from friends and family following discharge, actively letting people in, and developing trust in others. On the other hand, participants who had relapsed reported feelings of loneliness, isolation, and alienation, and a lack of social support. Thus, as well as exerting influence on a range of outcomes decades after diagnosis, it appears interpersonal functioning plays an important role in recovery from AN.

1.5 Candidate socio-cognitive mechanisms underlying interpersonal problems in AN

1.5.1 Social attention

A necessary precursor to social understanding and communication is social attention. In typical human development, social information in the environment is highly salient, and stimuli such as faces and eyes hold particular importance (Klein et al., 2009). An attentional bias towards social information is demonstrated from infancy, and reductions in this capacity are among one of the first signs of socio-communicative disorders such as ASD (Gliga & Csibra, 2007). Attending to nonverbal cues provided by others, such as eye gaze, gestures, and facial expressions, is key to higher-order social cognitive abilities. For example, given that different emotional expressions use different facial muscles, emotion recognition requires different patterns of attention to facial features. Indeed, eye-tracking research has demonstrated that gaze patterns differ depending on the valence of the emotion displayed; individuals attend more to the eyes of negatively valanced emotions and the mouths of positive emotions (Eisenbarth & Alpers, 2011). Abnormalities in social attention could therefore underlie difficulties in perception of nonverbal communication and social interaction in individuals with AN.

1.5.1.1 Reaction time (RT)-based paradigms

Several studies have examined social attention in individuals with AN using RT-based paradigms. These tasks are designed to measure attentional biases without conscious

awareness of the constructs of interest. For example, in the pictorial Stroop task (Ashwin et al., 2006), emotionally salient and neutral images are presented in different colours, and participants are instructed to identify the colour as quickly as possible. RTs to each picture are recorded. Increased RTs to one category of picture (e.g., angry faces) relative to another (e.g., chairs) are thought to indicate an attentional bias towards that type of stimuli, as the salience of the picture creates interference when completing the task (*interference effect*). Studies in individuals with AN have all used angry faces, neutral faces, and non-social stimuli (chairs), making it possible to examine both "social bias" (longer RTs to angry and neutral face stimuli relative to non-social stimuli) and "social-threat bias" (longer RTs to angry faces relative to neutral face stimuli). A few of these studies have found evidence of greater social and social-threat biases in individuals with AN compared to HCs (Harrison, Sullivan et al., 2010; Harrison, Tchanturia, & Treasure, 2010), however others have found no differences between groups (Goddard & Treasure, 2013; Kanakam et al., 2013).

The dot-probe task (Posner et al., 1980) has also been used to measure attention to socio-emotional stimuli in individuals with AN. In this task, a pair of face stimuli are presented to the left and right of the screen, followed by a probe (e.g., two dots) replacing one of the pictures. Participants are required to indicate which side of the screen the probe appeared on as quickly as possible. It is assumed that if the probe appears in the location of the image that was already being attended to, RTs will be faster than if the probe appears in the location that was not being attended to. Thus, faster RTs to probes in the location of one type of stimulus over another are indicative of increased attentional allocation. Again, findings from these studies are mixed, with some finding an attentional bias towards negative emotional faces and away from positive faces in individuals with AN (Cardi et al., 2012; Cardi, Esposito, et al., 2015), and others reporting similar patterns of attention in individuals with AN compared to HCs (Bang et al., 2017; Cardi, Corfield, et al., 2014; Schneier et al., 2016). The mixed findings here are likely due in part to the heterogenous methodology; few studies used the same stimuli, making comparisons across studies difficult. The population

under study also varied considerably across studies, with some including mixed ED groups, potentially reducing statistical power.

1.5.1.2 Eye-tracking studies

In addition to RT paradigms, a few studies have examined social attention using eye-tracking technology in individuals with AN. The following systematic review includes case-control studies that used eye-tracking in an ED sample. Because very few studies to date have used eye-tracking to measure social attention in this population, the review also includes those that examined food and body stimuli, as well as studies examining smooth pursuit and saccadic eye-movements. Most relevant to the current thesis are the studies discussed under section 3.3.3 'Social stimuli', however section 3.3.4 'Smooth pursuit and saccades' also contains important findings relating to possible alterations in the neuronal circuits that control eye-movements in individuals with AN. The supplementary material accompanying the review is presented in Appendix A.

Received: 31 July 2018 | Revised: 18 October 2018 | Accepted: 11 November 2018

DOI: 10.1002/eat.22998

WILEY

International Journal of EATING DISORDERS

REVIEW

Eye-tracking research in eating disorders: A systematic review

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Funding information
Economic and Social Research Council; Medical Research Council

Abstract

Objective: Those with eating disorders (EDs) show attentional biases to disorder-relevant stimuli, such as food and body shape information. However, attentional bias research in EDs largely relies on reaction time based measures, which are limited in their ability to assess different components and the time course of attention. Eye-tracking paradigms have therefore been utilized to provide greater ecological validity, and directly capture the detailed sequence of processes in perception and attention. While numerous studies have examined eye movements in the mood, anxiety, and psychotic disorders, there has been a lack of studies in EDs. The purpose of this qualitative review is to provide a summary of eye-tracking studies in clinical ED populations.

Method: The review was conducted using the PRISMA guidelines. Electronic databases were systematically searched to identify studies examining gaze parameters in ED compared to healthy controls (HCs). Thirty-one studies met inclusion criteria.

Results: Across ED diagnoses, there was evidence of attentional biases towards food and body stimuli. In addition, differential patterns of attention to social information, and differences in smooth pursuit and saccadic eye movements were found in anorexia nervosa (AN).

Discussion: Findings are discussed in relation to research in other psychiatric disorders, and recommendations for future studies using eye-tracking in EDs are given. The findings add to the wider literature on attentional biases in EDs, and provide potential avenues for treatment.

IJED-18-0331.R1.

Investigación de seguimiento ocular en trastornos de la conducta alimentaria: una revisión sistemática.

Resumen

Objetivo: las personas con trastornos de la conducta alimentaria (TCA) muestran sesgos de atención a los estímulos relevantes para el trastorno, como la información del alimento y figura corporal. Sin embargo, la investigación del sesgo atencional en los TCA depende en gran parte de las medidas basadas en el tiempo de reacción, que están limitadas en su capacidad para evaluar diferentes componentes y el curso temporal de la atención. Por lo tanto, los paradigmas de seguimiento ocular se han utilizado para proporcionar una mayor validez ecológica y capturar directamente la secuencia detallada de los procesos en la percepción y la atención. Si bien numerosos estudios han examinado los movimientos oculares en el estado de ánimo, la ansiedad y los trastornos psicóticos, ha habido una falta de estudios en los trastornos de la conducta alimentaria. El propósito de esta revisión cualitativa es proporcionar un resumen de los estudios de seguimiento ocular en poblaciones clínicas de trastornos de la conducta alimentaria.

Método: La revisión se realizó utilizando las guías PRISMA. Se realizaron búsquedas sistemáticas en las bases de datos electrónicas para identificar los estudios que examinaron los parámetros de mirada en los TCA en comparación con los controles sanos (HC). Treinta y un estudios cumplieron con los criterios de inclusión.

Resultados: En todos los diagnósticos de TCA, hubo evidencia de sesgos de atención hacia los estímulos alimentarios y corporales. Además, en la anorexia nervosa (AN) se encontraron patrones diferenciales de atención a la información social, y diferencias en la búsqueda suave y los movimientos oculares sacádicos.

Discusión: Los hallazgos se discuten en relación con la investigación en otros trastornos psiquiátricos, y se dan recomendaciones para futuros estudios que utilizan el seguimiento ocular en los TCA. Los hallazgos se suman a la literatura más amplia sobre los sesgos de atención en los TCA y proporcionan posibles vías para el tratamiento.

KEYWORDS

attentional biases, body image, eating disorders, eye gaze, eye movements, social perception

1 | INTRODUCTION

Eating disorders (EDs) are characterized by dysfunctional cognitions related to food, weight, and body shape (Fairburn, Cooper, & Shafran, 2003). These cognitions may bias attention to ED-related stimuli, such that negative body schemas result in individuals attending to schema-consistent stimuli, in turn reinforcing negative self-image and leading to negative emotions (Williamson, White, York-Crowe, & Stewart, 2004). In healthy women, body dissatisfaction and dietary restriction can be increased by inducing an attentional bias towards unattractive body parts and negative food words, respectively (Smith & Rieger, 2006, 2009). Furthermore, studies using attentional paradigms such as Stroop and dot-probe tasks have demonstrated that individuals with EDs show a bias towards negative food/eating stimuli compared to healthy and anxious controls (Renwick, Campbell, & Schmidt, 2013; Shafran, Lee, Cooper, Palmer, & Fairburn, 2007, 2008). Given that individuals with EDs also present with interpersonal difficulties (Treasure & Schmidt, 2013), attentional biases have also been studied in the context of social stimuli. In women with anorexia nervosa (AN) or bulimia nervosa (BN), an attentional bias towards angry and rejecting faces and away from neutral and compassionate expressions has been demonstrated (Cardi, Di Matteo, Corfield, & Treasure, 2012; Cardi, Di Matteo, Gilbert, & Treasure, 2014), and is associated with more emotion regulation difficulties (Harrison, Sullivan, Tchanturia, & Treasure, 2010). Further, these results have been replicated in individuals recovered from AN, suggesting that attentional biases towards threat may be a trait vulnerability factor (Harrison, Tchanturia, & Treasure, 2010).

Despite these findings, reaction time (RT) based measures (e.g., Stroop and dot-probe), are limited in their ability to assess different components of attention, such as differences in early automatic attention or attentional maintenance. Relatedly, it is difficult to distinguish the specific processes that are responsible for increased or decreased RTs. For example, in the emotional Stroop task, increased RTs for threatening stimuli are interpreted as hyper-vigilance (e.g., increased attention), as the emotional salience of the word interferes with the participants ability to make a response. However, it is also the case that avoidance (decreased attention) might be responsible, such that participants divert their attention away from the emotional stimulus, thereby increasing RTs (Aspen, Darcy, & Lock, 2013). Finally, RT based measures are also limited in their ability to measure attention in real-life visual environments, thus lacking ecological validity. For example, while dot probe tasks have allowed us to determine whether a particular stimulus is attended to over another, findings lack generalizability. They cannot tell us where an individual will attend during a mealtime, while looking at their body in a mirror, or during a social interaction. Understanding attention in such contexts will be vital in identifying potential factors that may maintain ED behaviors and cognitions.

Studies have therefore utilized eye-tracking paradigms to capture selection of information in real time, and the underlying processing strategies, in both healthy and psychiatric populations. Generally, such research involves measurement of two fundamental gaze parameters: fixations and saccades. Fixations represent points of attention, where gaze is held within 1° of the visual field for a duration of at least 100–300 ms (Toh, Rossell, & Castle, 2011). Saccades are rapid eye movements between fixations, shifting the focus from one point to another. A variety of processes can be inferred from these movements. For example, by measuring the latency of the first saccade towards a stimulus, or the relative proportion of trials in which the first saccade is made to a given stimulus, attentional engagement (early processing) can be measured. Similarly, attentional maintenance can be derived by calculating total duration or number of fixations to a stimulus, while saccade latency away from a stimulus can be taken as a measure of attentional disengagement (late processing).

Eye-tracking research can provide insights into cognitive, social, and emotional processes in psychiatric disorders. For example, in the social domain, both adults and children with autism spectrum disorder (ASD) spend less time looking at eye and face regions, and more time looking at non-social stimuli than healthy controls (HCs) (Frazier et al., 2017). These differences are associated with impairments in areas of social cognition, for example, less time spent looking at the eyes predicts impairments in recognizing fearful expressions in adults with Asperger's syndrome (Corden, Chilvers, & Skuse, 2008). Further, while viewing video clips, more time spent looking at objects predicts poorer social adjustment, while increased fixation on mouths predicts better social adjustment in young adults with ASD (Klin, Jones, Schultz, Volkmar, & Cohen, 2002). These data suggest that by fixating on non-social stimuli, individuals with ASD may miss important social cues. Avoidance of the eyes has also been reported in social anxiety disorder (SAD) (Horley, Williams, Gonsalvez, & Gordon, 2003; Moukheiber et al., 2010; Weeks, Howell, & Goldin, 2013). For example, while a longer delay to orient to the eyes is associated with ASD, quicker attentional disengagement from the eyes is associated with higher levels of social anxiety, in line with the vigilance-avoidance theory of attention (Kleberg et al., 2017; Weierich, Treat, & Hollingworth, 2008).

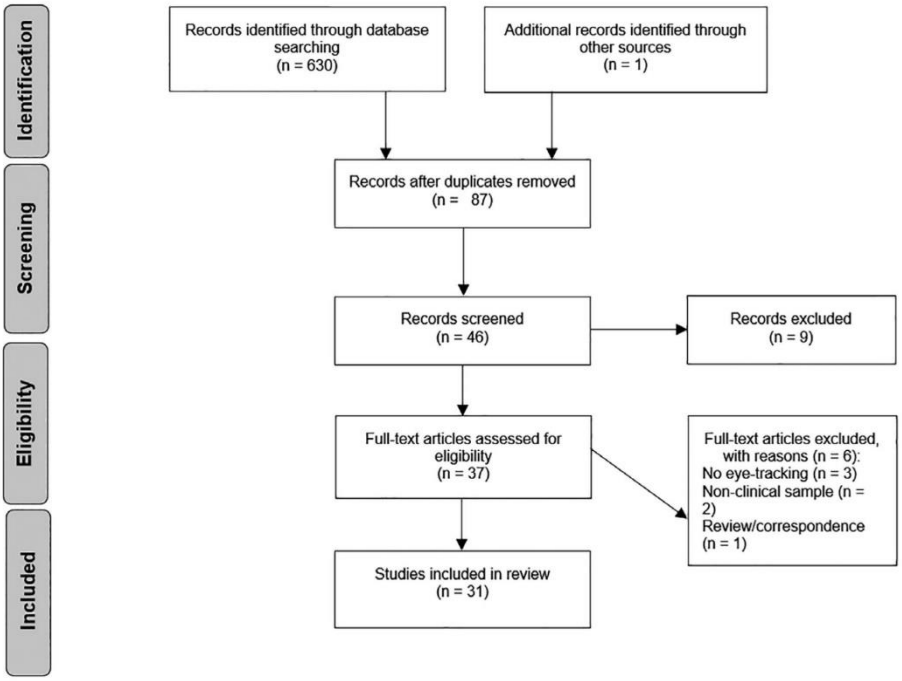

FIGURE 1 Systematic review search process

Despite numerous reviews of eye-tracking literature in psychiatric disorders such as those discussed above (Black et al., 2017; Chen & Clarke, 2017; Chita-Tegmark, 2016; Frazier et al., 2017; O'Driscoll & Callahan, 2008; Toh et al., 2011), no review to date has provided a synthesis of eye-tracking studies in EDs. Such a review will be important in understanding the cognitive and social mechanisms underlying the attentional biases seen in EDs. Therefore, the aim of this systematic review is to provide a summary of eye-tracking studies in clinical ED populations.

2 | METHOD

This review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009).

2.1 | Eligibility criteria

Studies were included if they used eye-tracking in a sample of individuals with a clinical ED, and included a HC group. Studies were also required to be published in a peer-reviewed journal and full text available. Studies investigating eye movement desensitization and reprocessing (EMDR) were not included.

2.2 | Information sources and search

Studies were identified by searching the electronic databases PubMed, PsycInfo, SCOPUS, and Web of Science up to and including June 2018. Search terms included anorexia nervosa OR bulimia nervosa OR eating disorder AND eye-tracking OR eye gaze OR eye movements. No search limits were applied.

2.3 | Study selection

Screening and selection of articles is displayed in Figure 1. Where titles of articles appeared relevant, abstracts were screened for eligibility, and full texts of potentially eligible studies were then retrieved. Any full texts that did not meet full eligibility criteria were excluded from the review.

2.4 | Data collection

Independent study searches were carried out by authors J.K.G. and A.H. The following information was extracted from each paper: number of participants in each group, mean age and body mass index (BMI), percentage of female participants, group matching technique, stimuli, and eye-tracking task used, outcome measures, and key findings.

2.5 | Risk of bias in individual studies

Risk of bias in individual studies was assessed using the Kmet form for quantitative analysis (Kmet, Lee, & Cook, 2004). The Kmet form assesses quality of studies on 14 criteria relating to the study design, methods, samples, reporting of results, and conclusions. Three of the criteria did not apply to studies included in this review. The remaining

TABLE 1 Characteristics of studies

Study	N and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Food stimuli									
Baldofski, Lüthold, Sperling, and Hilbert (2018)	19 NES (12 full-syndrome, 7 subsyndromal)	44.42 (13.15)	35.12 (9.28)	57.89	Age, sex, BMI	Food vs. non-food	1. Free viewing	1. Gaze direction bias	Group difference = ns. NES showed an initial orienting bias towards food stimuli, whereas HC did not.
	19 HC	44.68 (14.01)	35.54 (10.33)	57.89				2. Gaze duration bias	Group difference = ns. NES and HC fixated longer on non-food than food stimuli.
							2. Visual search task	1. Food detection bias score	Groups difference = ns.
Giel et al. (2011)	19 AN	24.4 (4.1)	15.8 (1.8)	NR	NR	Food vs. non-food	1. Free viewing	1. Gaze direction bias	Group differences = ns. All groups showed an initial tendency for food pictures, and this was strongest and significant in AN.
	18 HC (fasted)	24.4 (2.6)	21.6 (1.5)	100				2. Initial fixation duration bias	Group differences = ns. HC (fasted) showed a significant tendency to fixate on food pictures.
	20 HC (non-fasted)	24.2 (2.9)	21.3 (1.7)	100				3. Gaze duration bias	AN < HC (non-fasted) < HC (fasted). Both HC groups showed a significant tendency to continuously attend to food over non-food images.
Godier, Scaife, Braeutigam, and Park (2016)	13 AN-R	31.2 (5.3)	15.7 (1.9)	100	Sex	Food, low vs. high calorie	1. Responding to stimulus (black square)	1. X-span and Y-span	AN-REC > AN-R, HC. All groups explored high-calorie pictures more than low calorie pictures.
	14 AN-REC	27.1 (6.5)	20.9 (1.6)	100				2. P-span	AN-REC > AN-R, HC. All groups had larger pupil dilation in response to high calorie pictures compared to low calorie pictures.
	15 HC	23.7 (5.4)	21.4 (1.9)	100					

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Leehr et al. (2016)	21 BED	31.0 (12.3)	34.4 (5.5)	100	Age, sex	High calorie food vs. non-food	1. Antisaccade task (inhibitory control)	1. Number of 1st saccade errors	BED > obese controls, HC (food and non-food trials)
	23 obese controls	31.7 (11.2)	33.2 (4.2)	100					
	25 HC	31.4 (10.9)	22.3 (1.7)	100					
Leehr et al. (2018)	24 BED	31.46 (12.03)	34.93 (5.24)	100	Age, sex	High calorie food vs. non-food	1. Antisaccade task (inhibitory control) after negative mood induction	1. Number of 1st saccade errors	BED > overweight controls, HC (food and non-food trials).
	23 obese controls	28.39 (7.55)	32.99 (3.81)	100				2. Number of 2nd saccade errors	BED > HC (food and non-food trials considered together)
	26 HC	33.15 (12.63)	22.22 (1.77)	100					
Schag et al. (2013)	25 BED (22 full-syndrome, 3 subsyndromal)	39.7 (11.7)	35.4 (5.6)	100	Age, sex, BMI	Food vs. non food	1. Free viewing	1. Initial fixation position	Group differences = ns. All groups tended to initially fixate on food stimuli.
	26 overweight controls	39.9 (12.6)	35.4 (5.4)	100				2. Gaze duration bias	BED > overweight controls, HC. All groups tended to fixate longer on non-food than food stimuli.
	25 HC	39.4 (11.8)	22.5 (1.6)	100			2. Antisaccade task	1. First saccade errors	BED > overweight controls, HC (food and non-food trials). All groups made more errors in food trials than non-food trials.
								2. Second saccade errors	BED > overweight controls, HC (food trials only).
								3. Sequential errors	BED > overweight controls, HC (food and non-food trials).
Schmidt, Lüthold, Kittel, Tetzlaff, and Hilbert (2016)	25 BED	14.68 (2.85)	BMI-SDS 1.77 (0.95)	88	Age, sex, BMI, SES	Food vs. non-food	1. Free viewing	1. Gaze direction bias	Group differences = ns. Neither group showed a bias for food.
	25 HC	15.28 (2.39)	BMI-SDS 1.77 (0.82)	NR				2. Gaze duration bias	BED > HC (attractive food only).
							2. Visual search task	1. Detection bias score	BED > HC. BED were faster to detect food targets, while HC were faster to detect non-food targets.

(*Continues*)

TABLE 1 (Continued)

Study	N and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Sperling, Baldofski, Lüthold, and Hilbert (2017)	23 BED (17 full-syndrome, 6 subsyndromal)	35.30 (11.39)	32.40 (9.24)	65.2	Age, sex, BMI	Food vs. non-food	1. Free viewing	1. Gaze direction bias	Group differences = ns. Neither group showed a bias for food.
	23 HC	35.96 (12.20)	32.79 (9.01)	65.2				2. Gaze duration bias	BED > HC. Both groups showed a bias for non-food stimuli, however BED looked at food stimuli longer than HC.
							2. Visual search task	1. Detection bias score	Group differences = ns. In comparisons with full-syndrome BED only, there was a marginally significant tendency for BED > HC (faster detection of unattractive food stimuli), whereas HC did not show any bias.
Body stimuli									
Bauer, Schneider, Waldorf, Braks, et al. (2017)	30 AN-R	15.80 (1.09)	16.38 (1.36)	100	Sex	Body, self vs. other	1. Free viewing	1. Fixation times	AN-R < HC = AN-BP, BN, anxiety (attractive areas); AN-R > HC, anxiety = AN-BP, BN (unattractive areas). All groups looked longer at unattractive areas compared to attractive areas, and their own compared to others bodies.
	26 AN-BP	16.42 (0.85)	16.73 (1.37)	100					
	22 BN	16.72 (0.76)	20.91 (2.21)	100				2. Gaze duration bias for unattractive body parts	Bias for unattractive parts of ones own body were associated with subsequent lower body satisfaction in all groups. The same pattern for others bodies was seen in HC and anxious controls only.
	20 anxiety	15.94 (1.64)	19.98 (2.57)	100					
	43 HC	15.85 (1.77)	19.97 (2.44)	100					

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Bauer, Schneider, Waldorf, Cordes, et al. (2017)	56 AN	16.09 (1.03)	16.54 (1.36)	100	Sex	Body, self	1. Free viewing	1. Gaze duration bias for unattractive body parts	AN > HC in the first half (0-3, 000 ms) of stimulus presentation time only
	43 HC	15.85 (1.77)	19.97 (2.44)	100					
Blechert, Nickert, Caffier, and Tuschen-Caffier (2009)	20 BN	26.6 (7.68)	22.6 (3.40)	100	Sex	Body, self vs. other (lower vs. higher BMI)	1. Free viewing	1. Fixation times (% of total presentation time)	BN > HC (lower BMI bodies), BN < HC (high BMI bodies). Group differences for own bodies = ns.
	22 HC	26.5 (4.65)	20.3 (2.24)	100					
Blechert, Ansorge, and Tuschen-Caffier (2010)	19 AN	23.5 (4.66)	16.5 (1.35)	100	Sex	Body, self vs. other	1. Dot-probe task	1. First saccade latency	Group differences = ns. AN had significantly shorter saccade latencies for self trials compared to other trials (no difference in BN and HC).
	18 BN	26.9 (8.35)	22.9 (3.39)	100				2. Saccade difference score	In AN, faster saccades for self-photos were associated with lower satisfaction to the self-photo.
	21 HC	27.1 (4.77)	20.3 (2.12)	100					
Cornelissen, Cornelissen, Hancock, and Tovée (2016)	20 AN-WR	23.70 (4.43)	21.71 (3.95)	100	Sex, BMI	Body, other	1. Body size estimation in comparison to self	1. Fixation count (per cell)	Face: AN-WR > HC (acc), HC (over); central abdominal region: HC (acc) > AN-WR > HC (over). All groups spend longer looking at the abominal region than anywhere else.
	20 HC (accurate estimators)	23.25 (7.93)	23.01 (4.11)	100					
	20 HC (over-estimators)	20.60 (2.89)	23.19 (5.10)	100					

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Freeman et al. (1991)	15 AN or BN	21.9 (7.2)	16.5 (2.8)	100	Sex, age	Body, self	1. Free viewing	1. Fixation times (%)	Group differences not reported. In HC, there was a similar proportion of time spent looking at and satisfaction with each body region. In ED, patients spent more time looking at parts of their body they were dissatisfied with.
	10 HC	25.7 (8.1)	19.8 (3.1)	100				2. Evaluative gaze index	HC > ED
George, Cornelissen, Hancock, Kiviniemi, and Tovée (2011)	16 AN	26.2 (7.9)	16.8 (2.1)	100	Age, sex	Body, other	1. Attractiveness rating	1. Fixation count (per cell)	Centre rib cage: HC > AN; lower stomach and groin, upper chest and collar bone: AN > HC
	16 HC	26.1 (7.7)	22.8 (3.0)	100			2. Body size estimation		Upper stomach and lower rib cage: HC > AN; lower stomach and groin: AN > HC.
Horndasch et al. (2012)	17 AN or BN	16.0 (1.9)	18.6 (2.2)	100	Sex	Body, other	1. Free viewing	1. Fixation time	ED > HC (unclothed body parts). Both groups looked longer at "index areas" (hip, abdomen, buttocks, upper legs) than at the rest of the body.
	25 HC	15.3 (1.9)	21.3 (1.6)	100					
Phillipou, Rossell, Gurvich, Castle et al. (2016a)	24 AN	23.07 (6.88)	16.52 (1.14)	100	Age, sex, premorbid IQ	Point light walkers	1. Implicit task—gender identification	1. Fixation count	AN > HC. In AN, fixation count increased for mid-heavy size male stimuli relative to female stimuli. Fixation count to male and female stimuli did not differ in HC.

(*Continues*)

TABLE 1 (Continued)

Study	N and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
	24 HC	22.72 (3.25)	22.26 (3.59)	100			2. Explicit body size estimation	2. Fixation duration	AN < HC. Longer fixations were made to both thin and heavy stimuli than other sizes, and during the implicit task compared to the explicit task.
								3. Saccade amplitude	AN < HC (implicit task). Larger amplitudes were found for found for thin and thin-mid body sizes, and male stimuli.
Svaldi, Caffier, and Tuschen-Caffier (2011)	26 BED	44.2 (9.56)[a]	38.7 (8.22)	100	Sex	Body, self vs. other	1. Free viewing	1. Fixation count	BED > overweight controls (ugliest self body part); BED > overweight controls (ugliest other body part). Both groups looked at ugly body parts more frequently than beautiful parts (self and other stimuli).
	18 overweight controls		30.0 (3.80)	100				2. Fixation times	BED > overweight controls (ugliest self body part); BED > overweight controls (ugliest other body part). Both groups looked at ugly body parts for longer than beautiful parts (self and other stimuli).
Svaldi, Caffier, and Tuschen-Caffier (2012)	23 BED	40.33 (11.6)[a]	37.7 (6.85)	100	Sex	Body, self vs. other	1. Cued for self stimuli vs. no cue (instruction/task not reported)	1. 1st fixation direction (frequency)	Cued condition: BED > overweight controls (self stimuli); BED < overweight controls (other body).

(*Continues*)

TABLE 1 (Continued)

Study	N and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
	23 overweight controls		29.8 (3.94)	100				2. 1st fixation duration	Group differences = ns.
								3. 2nd fixation direction (frequency)	Cued condition: BED > overweight controls (self stimuli); BED < overweight controls (other body).
								4. 2nd fixation duration	Cued condition: BED < overweight controls (other body). Overall, fixations were longer for self stimuli than other bodies.
Svaldi et al. (2016)	12 AN	15.14 (1.55)	18.13 (1.46)	100	Age, sex	Body, self (mirror)	1. Free viewing (2 conditions: Postive and negative mood induction)	1. Fixation times	AN > HC (most ugly body part, negative mood condition). AN looked longer at the most ugly than the most beautiful body part in both positive and negative mood inductions, while HC looked longer at the most ugly part in the positive mood induction only.
	12 HC	15.15 (1.57)	20.56 (2.29)	100				2. Gaze frequency	AN > HC (most ugly body part, negative mood condition). AN looked more frequently at the most ugly than the most beautiful body part in both mood inductions. HC showed a trend to look more frequently at the most ugly part in the positive mood induction only.

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Tuschen-Caffier et al. (2015)	16 AN	22.09 (3.29)	14.55 (1.15)	100	Sex	Body, self (mirror)	1. Free viewing	1. Fixation times	Group differences not reported. AN and BN spent more time looking at their most dissatisfying and ugly body parts than satisfying and beautiful parts. In HC, there were no differences.
	16 BN	22.31 (6.00)	21.10 (2.92)	100				2. Gaze frequency	Group differences not reported. AN and BN looked more frequently at their most dissatisfying and ugly body parts than satisfying and beautiful parts. In HC, there were no differences.
	16 HC	23.65 (1.34)	21.41 (2.80)	100					
Von Wietersheim et al. (2012)	35 AN	22.9	16.4	100	Sex	Body, self vs. other	1. Free-viewing	1. Fixation times (as a proportion of a total)	AN < HC (breasts of other body stimuli); AN > HC (thighs of own body). In AN, those who rated their abdomen as less attractive fixated on it longer. In HC, those who rated their thighs as less attractive fixated on them longer.
	32 HC	22.2	21.5	100				2. Fixation count	AN < HC (breasts of own body)
Social stimuli									
Fujiwara, Kube, Rochman, Macrae-Korobkov, and Peynenburg (2017)	24 AN or BN	23.33 (7.12)	19.3	100	Sex	Faces, blended emotions	1. Emotion discrimination	1. Dwell time	Angry and disgust faces: ED < HC-LA, HC-HA. In ED shorter dwell time predicted more difficulty judging ambiguous anger and disgust faces.
	25 HC (high alexithymia)	18.60 (2.04)	NR	100				2. Eye-preference	Group differences = ns. In ED less attention to the eyes predicted more difficulty judging ambiguous anger and disgust faces.
	25 HC (low alexithymia)	19.92 (3.8)	NR	100				3. Saccades	Group differences = ns.

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Kollei, Horndasch, Erim, and Martin (2017)	21 BN	23.67 (4.31)	20.91 (2.15)	100	Sex	Face, self vs. other	1. Free viewing	1. Dwell time	HC > BDD, BN (most attractive facial feature, self); BDD ≥ BN ≥ HC (least attractive facial feature, self). Group differences for other faces = ns.
	19 BDD	23.79 (4.25)	21.84 (2.93)	100				2. Fixation count	Main effect of group for least attractive facial part (self), but group differences = ns. Group differences for other faces = ns.
	21 HC	23.52 (2.84)	22.25 (2.93)	100					
Phillipou et al. (2015)	23 AN	22.18 (5.45)	16.47 (1.13)	100	Sex	Faces, self vs. other	1. Implicit task—gender identification	1. Fixation count	AN > HC. Both groups made a greater number of fixations to their own faces and faces depicting anger and fear.
	24 HC	22.64 (3.25)	22.36 (3.66)	100			2. Explicit emotion identification task	2. Fixation duration	AN < HC.
								3. Saccade amplitude	Group differences = ns.
								4. Feature fixation index (FFI) and feature duration index (FDI)	HC > AN. FFI and FDI were higher for participants own faces, and faces depicting anger, disgust, fear, and sadness. Salient features were also attended to more during the implicit task compared to the explicit task.
Pinhas et al. (2014)	13 AN	14.5 (1.61)	90.1% IBW	100	Age, sex	Thin body shapes (TBS) vs. fat body shapes (FBS) vs. social interactions	1. Free viewing	1. Relative fixation times (%)	AN > HC (TBS & FBS); AN < HC (social images). AN spent more time looking at both thin and fat body shapes than social images, and more time looking at thin compared to fat body shapes. HC spent similar amounts of time on all 3 types of image.

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
	20 HC	14.4 (1.82)	NR	100				2. Fixation count	AN: TBS > social images; FBS > social images. HC: TBS = social images; FBS = social images.
								3. Fixation duration	AN: TBS > social images; FBS > social images. HC: TBS = social images; FBS = social images.
Watson, Werling, Zucker, and Platt (2010)	11 AN-WR	NR	NR	100	Sex	Faces vs. bodies, other	1. Free viewing	1. Dwell time	Faces: AN-WR < HC (when bodies were also present). Eyes: AN-WR < HC (when faces presented alone). Participants looked at faces of extremely thin females less than faces of other weight classes.
	11 HC	NR	NR	100					
Smooth pursuit and saccades									
Pallanti, Quercioli, Zaccara, Ramacciotti, and Arnetoli (1998)	28 AN-WR	23.9 (3.4)	NR	100	Age, sex, education	Horizontal arcs	1. Smooth pursuit	1. Typical target velocity	AN < HC
	28 HC	24.4 (3.8)	NR	100				2. Typical matching target velocity	AN < HC
								3. Anticipatory saccades (total number)	AN > HC
								4. Anticipatory saccades (total amplitude)	AN > HC
								5. SWJ rate	Group differences not reported. SWJ were present in 10.7% of AN and 0% of HC.

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Phillipou, Rossell, Castle, Gurvich, and Abel (2014)	23 AN	23.14 (7.03)	16.54 (1.16)	100	Age, sex, premorbid IQ	Fixation cross	1. Fixation task	1. SWJ rate	AN > HC
	22 HC	22.94 (3.23)	22.70 (3.63)	100					
Phillipou, Rossell, Gurvich, Hughes et al. (2016b)	24 AN	23.07 (6.88)	16.52 (1.14)	100	Age, sex, premorbid IQ	Dots	1. Self-paced saccades	1. Saccade rate	Group differences = ns.
	24 HC	22.67 (3.19)	22.4 (3.59)	100				2. Gain	Group differences = ns.
								3. Intersaccadic interval	Group differences = ns.
								4. Peak velocity	Group differences = ns.
							2. Memory-guided saccades	1. Gain	Group differences = ns.
								2. Latency	Group differences = ns.
								3. Peak velocity (5°, 10° targets)	Group differences = ns.
								4. Inhibitory error rate (5°, 10° targets)	AN > HC (10° targets)
								5. Directional error rate	Group differences = ns.
							3. Pro-saccade / antisaccade/ no-go task	1. PAN error rate	Group differences = ns.
								2. Prosaccade gain	Group differences = ns.
								3. Prosaccade latency	AN < HC
								4. Prosaccade peak velocity (5°, 10° targets)	Group differences = ns.
								5. Antisaccade gain	Group differences = ns.
								6. Antisaccade latency	Group differences = ns.
								7. Antisaccade peak velocity (5°, 10° targets)	Group differences = ns.

(*Continues*)

TABLE 1 (Continued)

Study	*N* and group	Mean age (SD)	Mean BMI (SD)	% female	Groups matched by	Stimuli	Eye-tracking task	Outcome measures	Main findings
Other									
Giel et al. (2013)	15 AN	23.9 (4.9)	15.4 (1.7)	100	Age, sex	Pictures depicting physical activity vs. inactivity	1. Free viewing	1. Gaze direction bias	Group differences = ns. All group showed a tendency to first attend to active stimuli.
	15 athletes	24.5 (3.0)	21.8 (1.8)	100				2. Gaze latency bias	Group differences = ns. All groups showed a tendency to orient their attention quicker to active than inactive stimuli.
	15 HC	24.7 (2.8)	21.3 (1.5)	100				3. Gaze duration bias	HC < AN, athletes. AN and athletes looked longer at active stimuli, whereas HC looked at active and inactive stimuli for similar lengths of time.

AN = anorexia nervosa; AN-BP = anorexia nervosa binge purge sub-type; AN-R = anorexia nervosa restricting sub-type; AN-REC = recovered AN; AN-WR = weight-restored anorexia nervosa; BDD = body dysmorphic disorder; BED = binge-eating disorder; BMI = body mass index; BMI-SDS = body mass index standard deviation score; BN = bulimia nervosa; ED = eating disorder; HC = healthy control; IBW = ideal body weight; IQ = intelligence quotient; NES = night eating syndrome; NR = not reported; ns = not significant; PAN = pro-saccade /antisaccade/no-go; RT = reaction time; *SD* = standard deviation; SES = socioeconomic status; SWJ = square wave jerk.

[a] Only reported for groups combined.

11 criteria are scored 0, 1, or 2, resulting in a maximum score of 22 (see Supporting Information 1).

2.6 | Synthesis of results

Studies were grouped by the type of stimulus used in the eye-tracking task: food, bodies, social, and smooth pursuit and saccades. The three former categories are commonly used in attention research, while smooth pursuit and saccades are unique to eye-tracking research. Findings are summarized with respect to differences between groups on specific outcome measures.

3 | RESULTS

3.1 | Study selection

Thirty-one studies were included in the review (Table 1). Two studies also included another psychiatric group (anxiety disorders and body dysmorphic disorder). Eighteen studies included an AN group, two of which were weight restored (AN-WR), and one which compared recovered and acute groups. Five studies included a BN group, seven included a binge-eating disorder (BED) group, one included a night eating syndrome (NES) group, and three studies included a mixed group of AN and BN. Two pairs of studies used the same sample for at least one group. Phillipou et al. (2016) and Phillipou et al. (2016) used the same AN sample, while Bauer et al. (2017) and Bauer et al. (2017) used the same HC sample. Due to the different processes and research questions being studied, the results from these studies are presented separately.

3.2 | Study characteristics

Overall, reporting of study characteristics was good, with Kmet scores ranging from 13 to 21. All but one study (Watson et al., 2010) reported mean age of participants (range: 14.4–44.68 years), and only four studies did not report the mean BMI or % ideal body weight (IBW) of at least one participant group (Fujiwara et al., 2017; Stefano Pallanti et al., 1998; Pinhas et al., 2014; Watson et al., 2010). Most studies used exclusively female samples, however three studies examining either NES or BED included male participants (Baldofski et al., 2018; Schmidt et al., 2016; Sperling et al., 2017). A wide variety of tasks were employed, the most common being free-viewing, where participants are asked to simply view stimuli as if they were watching television. Similarly, many different outcome measures were reported, often several within the same study (see Supporting Information 2 for descriptions of outcome measures). All but one study (Giel et al., 2013) fell into one of the four main categories used to group studies.

3.3 | Synthesis of results

3.3.1 | Food stimuli

Of the eight studies that used food stimuli, five included individuals with BED. Three studies used an antisaccade task, designed to measure the impulsivity component of inhibitory control (Leehr et al., 2016, 2018; Schag et al., 2013). In this task, a high caloric food picture or a non-food picture is presented on one side of the computer screen, and participants are instructed to look at the opposite side of the screen as quickly as possible after stimulus onset. In all three studies, individuals with BED made significantly more incorrect first saccades (looked to rather than away from the stimulus) than both weight-matched and normal weight HCs, who did not differ from one another. In Schag et al. (2013), all groups made more errors in food compared to non-food trials, however this was only true for the HC group in Leehr et al. (2018), and there was no effect of trial in Leehr et al. (2016). In addition, Schag et al. (2013) and Leehr et al. (2018) measured second saccade errors, where a similar pattern was observed. In the former study, participants with BED made more second saccade errors in food trials than both weight-matched and normal weight HC, whereas in the latter, BED only committed more second saccade errors when food and non-food trials were considered together. Thus, it seems that while those with BED have difficulties in inhibitory control, evidence is mixed as to whether these difficulties are general or specific to food stimuli.

Three studies examined attention to food versus non-food stimuli in adults (Schag et al., 2013; Sperling et al., 2017) and adolescents (Schmidt et al., 2016), during both free-viewing and visual search tasks. During free-viewing, pairs of food and non-food stimuli were presented for 3,000 ms. Across all three studies, there were no group differences in gaze direction bias. In both Schmidt et al. (2016) and Sperling et al. (2017), the groups did not show any bias towards either type of stimuli, however Schag et al. (2013) report that both participants with BED and HC tended to initially fixate on food stimuli. Regarding gaze duration bias, both participants with BED and HC tended to fixate on non-food stimuli longer than food stimuli. However, those with BED fixated on food stimuli longer than control groups in all three studies. Thus, while initial attention to food does not seem to differ in adults and adolescents with BED, there is increased attention when overall looking times are considered. In the visual search task, arrays of food and/or non-food images are presented, and participants are required to indicate whether all images are of the same category or whether one image is different. Adolescents with BED were faster to detect food targets, while HCs were faster to detect non-food targets (Schmidt et al., 2016). However, in adults, no significant group differences were found (Sperling et al., 2017). Using the same free-viewing and visual search tasks, Baldofski et al. (2018) examined whether individuals with NES show similar patterns of attention to food as those with BED. No significant group differences were found in gaze direction or duration bias (free-viewing), or food detection bias (visual search). However, participants with NES did show an initial orienting bias to food stimuli in the free-viewing task (HC did not), and a marginally significant food detection bias in the visual search task when only those with full-syndrome NES were considered (HC did not).

Two studies examined attention to food stimuli in participants with AN. The first used a similar free-viewing paradigm to that used in BED and NES (Giel et al., 2011). Importantly, two control groups were included (a satiated group and an 8-hr fasted group), to control for fasting-related effects on attention. Similar to what was found in individuals with BED, there were no significant group differences in the proportion of initial fixations to food versus non-food pictures.

However, despite all three groups showing a tendency to initially orient toward food pictures, this tendency was significant in participants with AN only. Again, there were no significant group differences regarding the duration of initial fixations, however fasted HCs showed a tendency to initially fixate longer on food pictures. Finally, regarding total gaze duration, significant differences were found across groups. HCs looked at food pictures longer than control pictures (fasted HC more so than satiated HC), whereas AN showed similar shorter gaze durations for the two categories of pictures.

The second study used eye-tracking, RTs, and magnetoencephalography (MEG) to investigate the temporal dynamics of food processing in participants with AN (acute and recovered) compared to HCs (Godier et al., 2016). Pictures of low or high calorie food were presented for 4,000 ms, during which time a small square would appear centrally between 500 and 1,500 ms after stimulus onset. Participants were required to respond with a button press. While there were no group differences in RTs, the recovered AN group showed significantly more exploration (defined by deflection across the *x* and *y* axis from the central point) of the pictures, as well as increased pupil size compared to the other two groups. There was also a main effect of calorie, whereby high calorie foods were explored more than low calorie ones. Regarding neural responses, there were two time points where group differences reached significance—150 ms (posterior regions, AN > AN-REC, HC) and 320 ms (occipital regions, AN-REC > AN, HC). The increase in neural activity in the recovered group may reflect an increase in the visual P300 component, modulation of which is related to emotional/motivational properties of visual stimuli (Hajcak, MacNamara, & Olvet, 2010).

3.3.2 | Body stimuli

Self versus other bodies

Fourteen studies investigated attention to body stimuli, several of which examined attention towards photographs of one's own body compared to others' bodies. Using a modified dot-probe task, Blechert et al. (2010) presented participants with AN, BN, and HCs with photographs of their own body alongside those of another body. Shortly after the picture pair was presented, colored frames would appear around the photographs, and participants had to indicate the photograph with the target color by making a saccade towards it. Saccade latency was therefore taken as a more ecological, covert measure of attention than the more frequently used button-press. Those with AN showed significantly shorter saccade latencies towards their own body than other bodies, whereas those with BN and HC did not show any attentional bias. In a similar paradigm, Svaldi et al. (2012) compared individuals with BED and overweight controls. Different from the previous study, trials were either cued, where participants were told which side their own body photo would appear on, or not cued, however they received no instruction of where they should look. The authors propose that the cued condition would prime participants to think of their own body, therefore activating body-related schema. Overall, first and second fixations were more often directed to and were longer for self pictures. However, those with BED directed both first and second fixations more often to self pictures than controls, and their second fixations towards other bodies were significantly shorter than those of controls. Importantly, these effects were only found in the cued condition, suggesting that the attentional bias found in BED may be a result of activation of body-related schemas, rather than automatic processes.

In contrast to the above findings, two studies did not find group differences in attention to self versus other bodies. Bauer, Schneider, Waldorf, Braks, et al. (2017) presented photographs of participants' own bodies and other bodies one at a time during free-viewing. Participants were adolescents with AN, BN, clinical controls with anxiety disorders, and HCs. All groups fixated longer on their own body compared to other body pictures. Finally, a study by Blechert et al. (2009) examined social comparison strategies in participants with BN and HC. Trials consisted of a photograph of the participants' own body, with three lower and three higher BMI bodies alongside. Similar to previous findings in BN, there were no group differences in attention to self bodies. While no direct comparison of attention towards self versus other bodies was carried out, it was found that attention to other bodies differed as a function of that body's BMI in those with BN. Participants with BN looked significantly longer at low BMI bodies, and significantly less at high BMI bodies than HCs. Although participants were not explicitly instructed to compare the bodies shown, the authors suggest that individuals with BN engage in more downward social comparisons. Further, there was a significant decline in body satisfaction scores from pre- to post-testing in the BN group (while it increased in HC), lending support for social comparison theory.

Attractive versus unattractive body parts

Several studies examined attention to body parts participants deemed attractive or unattractive. Importantly, attractiveness ratings are made after the eye-tracking task, to ensure that attention is not biased by the judgements. These studies consistently show that when looking at their own bodies, participants with AN and BN pay more attention to parts of their body they rate as most unattractive, compared to HC. For example, during free-viewing, those with AN and BN spend significantly more time looking at parts of their body they are dissatisfied with, while HC spend a similar proportion of time looking at satisfactory and unsatisfactory body parts (Freeman et al., 1991; Tuschen-Caffier et al., 2015). Interestingly, in participants with AN, there is evidence that this bias appears only in the early stage of processing. To investigate whether those with AN show threat-related patterns of attention (early vigilance and later avoidance), Bauer, Schneider, Waldorf, Cordes, et al. (2017) measured the time course of attention while participants viewed pictures of their own body. Twelve body areas of interest (AOIs) were drawn individually for each body picture, following a standardized procedure in terms of area definition. Pictures were presented for 6,000 ms, and fixation times to unattractive areas (relative to overall fixation times) were measured across six 1,000 ms intervals. It was found that attention to unattractive areas was significantly higher in AN than HC in the first 3,000 ms only. Furthermore, attention to unattractive body parts significantly decreased over time in those with AN, while in HC, there was no change over time. These findings indicate an automatic, pre-

intentional pattern of attention to unattractive areas of one's own body in AN.

In another study comparing participants with AN and HC, the effects of mood on attention to attractive and unattractive body parts was examined (Svaldi et al., 2016). Participants received a positive or negative mood induction (recalling an event from the past few weeks), then eye movements were tracked while viewing their bodies in a mirror for 3 min. In the positive mood condition, both groups looked longer and more frequently at their most unattractive body parts than attractive parts. However in the negative condition, only individuals with AN looked significantly longer at their most unattractive part compared to their most attractive part, while attention was balanced in HCs. It is suggested that HC may engage in some form of "mood-repair" in response to the negative mood induction, perhaps by paying more attention to neutral or positive body information. However in those with AN, attention to negative information is increased by negative mood, thus reinforcing negative body schemas.

Bauer, Schneider, Waldorf, Braks, et al. (2017) examined whether a bias for unattractive body parts was also present when looking at other's bodies. The procedure used in Bauer, Schneider, Waldorf, Cordes, et al. (2017) was used to map AOIs. Across groups (adolescents with AN, BN, anxiety disorders, or HC), participants attended to unattractive body areas longer than attractive areas for both self and other bodies, however this preference was stronger for one's own body. Further, those with AN-R looked at unattractive parts significantly longer, and attractive parts less than controls, however this effect was for bodies overall rather than their own body specifically. These results are in contrast with those of the aforementioned studies, who generally found weaker or no attentional biases in HC (Bauer, Schneider, Waldorf, Cordes, et al., 2017; Freeman et al., 1991; Svaldi et al., 2016; Tuschen-Caffier et al., 2015). Instead, they suggest that adolescents, with or without EDs show a general bias for unattractive body areas, especially for their own bodies. This question has also been investigated in those with BED. Svaldi et al. (2011) presented women with BED and HCs with photos of their own body alongside a BMI matched control photo. Both groups looked at the most unattractive body part longer and more frequently than the most attractive body part of both self and control bodies, however, this tendency was stronger in those with BED compared to HC. Thus, like other EDs, a stronger attentional bias towards unattractive body parts is apparent in individuals with BED.

Making judgements on attractiveness and body size

In contrast to the above studies, a few studies aimed to examine which parts of the body those with AN and HC looked at when making attractiveness and body size judgements. Importantly, these studies used a novel approach to mapping AOIs to increase spatial resolution. All body images were morphed together to produce a reference image, and fixations can then be transformed into a heat map displaying fixation densities across the body. George et al. (2011) found that when judging the attractiveness of photographs of other bodies, those with AN made significantly more fixations to the lower stomach, groin, upper chest, and collar bone, while HC fixated more on the center of the rib cage. When estimating body size, participants with AN made significantly more fixations to the lower stomach and groin, whereas HCs fixated more on the upper stomach and lower region of the rib cage. Cornelissen et al. (2016) examined whether the pattern of eye movements displayed in those with AN is specific to those with the disorder, or whether it is also present in healthy individuals who overestimate body size. It was found that while all groups (AN-WR, over-estimating HC, and accurate HC) spent most time looking at the abdominal region of others' bodies, AN-WR looked at this area significantly less than accurate HCs, but significantly more than over-estimating HCs. Further, AN-WR looked significantly longer at the face than both HC groups. Thus, in agreement with George et al. (2011), accurate body size estimation is associated with more time spent looking at the abdominal region, whereas a more dispersed pattern of fixations up along the torso and onto the face may be specific to those with AN.

The final study to examine eye movements during body size estimation took a different approach, using point-light walkers (Phillipou, Rossell, Gurvich, Castle, et al., 2016). These stimuli represent biological motion through the movements of a few points representing the major joints of the body. Walkers were either male or female, and varied in body size. To investigate whether the explicit instruction to estimate body size would influence eye movements, both an explicit task (body size estimation) and an implicit task (gender discrimination) were included. In contrast to the results of George et al. (2011) and Cornelissen et al. (2016), individuals with AN and HC did not differ in the parts of the body fixated on during either task. There were also no group differences in accuracy of body size judgments or gender discrimination. The lack of overestimation of body size in the AN group may be a result of them looking at the same parts of the body as HCs when making their judgements, different from the previous studies. Although groups did not differ in where they looked, there were differences in how they looked—those with AN showed an increased number of fixations of shorter duration during both tasks. This may be evidence of "hyper-scanning"; a type of scanning behavior associated with anxiety disorders (Horley, Williams, Gonsalvez, & Gordon, 2004).

3.3.3 | Social stimuli

Five studies examined attention while viewing social stimuli. Similar to several of the body-related attention studies, Kollei et al. (2017) examined attention to attractive versus unattractive parts of one's own and other's faces in participants with BN, body dysmorphic disorder (BDD), and HC. Participants viewed photographs of their own and other female faces, and afterwards rated the attractiveness of parts of the faces. While HC spent similar amounts of time looking at attractive and unattractive features of both their own and other faces, participants with BN or BDD spent less time looking at attractive features of their own face than HC. Further, BDD and BN spent more time looking at attractive features compared to unattractive features of other faces. The findings indicate a possible neglect of positive aspects of one's own face in BDD and BN, and/or an upward social comparison strategy. Such a strategy may be responsible for the increase in negative emotions seen in BN and BDD (but not HC) after image viewing.

Extending previous work demonstrating an attentional bias to bodies in those with AN (Dobson & Dozois, 2004; Shafran et al., 2007), Pinhas et al. (2014) aimed to examine whether this bias would persist when bodies were presented alongside pictures of social interactions, a class of stimuli that is typically rewarding. When presented together, participants with AN showed a hierarchy of attention allocation, looking more at thin body shapes, followed by fat body shapes, and finally social interactions. In contrast, HC spent similar amounts of time on all three types of image, and significantly less time on body shape images than those with AN. Thus, when social and body images are competing for attention, individuals with AN show an attentional bias towards bodies, especially thin ones. However, a question remains over whether there is abnormal processing of social stimuli in the absence of such disorder-related stimuli. Watson et al. (2010) presented AN-WR and HCs with images of faces, or whole body images including faces. Those with AN-WR looked less at faces when the body was also present within the image compared to controls, thus showing an attentional bias towards body stimuli. Importantly, when faces were presented alone, AN-WR looked significantly less at the eyes than HC, providing the first eye-tracking evidence for abnormal processing of social stimuli in AN (without the influence of body/shape stimuli). These results were further clarified in a monetary choice task. In each trial, participants were given a choice between a constant cash payout, or a variable payout which would also show the face or body stimulus. It was found that AN-WR assigned higher monetary values to thin bodies, while reward value of body pictures was uninfluenced by weight in HC. In addition, HC consistently sacrificed money to see face stimuli, while AN-WR did not. Taken together, these results suggest that while HC show approach behavior to social stimuli, AN-WR tend to be indifferent or avoid viewing the faces or eyes of others.

Two studies examined eye movements during facial emotion recognition. The first (Phillipou et al., 2015) used Ekman faces displaying the seven basic emotions (anger, disgust, fear, happiness, sadness, surprise, and neutral), as well as photographs of participants' own faces while they were asked to hold a neutral expression. Adults with AN were just as accurate as HCs in recognizing the facial expressions of others, but were more likely to misidentify their own face as showing sadness. Regarding eye movements, those with AN showed an increased number of fixations of shorter duration to faces in general compared to HC, similar to the hyper-scanning behavior found by Phillipou, Rossell, Gurvich, Castle, et al. (2016). Thus, it is possible that faces may also be anxiety-provoking to individuals with AN. Lending some support for this possibility, participants with AN avoided salient features (eyes, nose, and mouth) of their own face compared to HC, however this effect was not found for other's faces. Building on this study, Fujiwara et al. (2017) investigated whether differences in eye movements might drive potential difficulties in facial emotion recognition commonly found in those with EDs (Caglar-Nazali et al., 2014). To control for the role of alexithymia in emotion recognition, both a high- and a low-alexithymia HC group, as well as a mixed group of participants with AN or BN were included. In each trial, participants were asked to estimate the mixture ratio of two emotional expressions blended into one face on a visual analogue scale. In contrast to Phillipou et al. (2015), those with EDs were less accurate at judging ambiguous angry and disgust expressions compared to HCs (particularly those with low alexithymia). Importantly, difficulty in judging anger and disgust in participants with ED was predicted by avoidance of these faces, in particular the eye region. When ED differed from HC, group differences tended to be significant only compared with HC-LA, with performance of HC-HA lying between the two. This, along with the finding that visual attention was linked to performance in the ED group only, suggests that alexithymia is not solely responsible for difficulties in emotion recognition.

3.3.4 | Smooth pursuit and saccades

Three studies have measured smooth pursuit parameters and/or saccadic eye movements in individuals with AN. In contrast to saccades, smooth pursuit is the process by which a moving stimulus is followed by the eyes in a slow, smooth eye movement. These eye movements have been useful in understanding the neurobiology of a variety of psychiatric disorders, as they are governed by known brain regions. For example, the superior colliculus (SC) is involved in the initiation and inhibition of saccades. Activity here is negatively related to saccade latency, such that the higher the activity of the SC, the faster the saccade to a target (Bittencourt et al., 2013). Smooth pursuit involves integration of activity from the frontal eye fields (FEF), visual and vestibular circuitry, cerebellum, thalamus, and the muscles and neural circuitry directly responsible for eye-movement (Gottesman & Gould, 2003).

Pallanti et al. (1998) aimed to examine links between eye movement parameters during smooth pursuit and clinical features. In each trial, a target moves in a horizontal arc at a constant speed, which the participant follows while their eye movements are recorded. Target speed differs across trials. AN-WR displayed a larger drop-off in performance as target speed increased compared to HC, and a greater number and total amplitude of anticipatory saccades (anticipatory jumps ahead of the target). While eye movements were not related to BMI, weight lost, length of illness, global psychopathology, or depression, poorer smooth pursuit performance was associated with OCD symptoms and ED psychopathology (perfectionism, drive for thinness, and interoceptive awareness).

Saccadic eye movements can also be studied during fixation on a stationary target. While some saccadic intrusions occur during fixation in the healthy population, increased rates have been found in both neurodegenerative and psychiatric disorders (Bittencourt et al., 2013; Terao, Fukuda, & Hikosaka, 2017). Phillipou et al. (2014) examined the incidence of square wave jerks (SWJs), the most widely studied saccadic intrusion, in participants with AN and HC. While fixating on a central cross, those with AN made significantly more SWJs than HC. In addition, more SWJs were associated with lower anxiety scores in the AN group only. It is suggested that γ-aminobutyric acid (GABA) has a role in lowering anxiety, as shown by anxiolytic treatments such as benzodiazepines being used to enhance GABA activity in anxious individuals (Tallman, Paul, Skolnick, & Gallager, 1980). Higher GABA activity in areas containing fixation neurons such as the SC and FEF may result in increased SJWs and difficulty maintaining fixation, providing a potential explanation for the association with anxiety in this group.

A final study used a battery of saccadic eye movement tasks, including self-paced saccades, memory guided saccades, and a prosaccade/antisaccade/no-go (PAN) task (Phillipou, Rossell, Gurvich, Hughes, et al., 2016). In the memory-guided saccade task, inhibitory error rates were higher in those with AN than HC, indicating a failure to inhibit reflexive responses. Further, in the PAN task, latency of correct prosaccades (saccades towards the stimulus) was significantly shorter in the AN group. Taken together, the results indicate potential functional alterations in the neuronal circuits that control eye movements in those with AN, however replications are required.

4 | DISCUSSION

The aim of this review was to provide a qualitative synthesis of studies that have utilized eye tracking in ED samples. Studies mostly examined attention to disorder-related stimuli; namely food and bodies, and found a variety of differences between ED and HC on specific outcome measures. A small number of studies also examined eye-movements while viewing social stimuli, while a few others examined smooth pursuit performance and saccadic eye-movements. Some key findings will be discussed here.

Several studies provided evidence for differential attention to images of food in individuals with ED compared to HC. Firstly, those with BED showed more difficulty in inhibiting their automatic attention to both food and non-food stimuli compared to HC (Leehr et al., 2016, 2018; Schag et al., 2013), as well as delayed disengagement to food stimuli, indicating increased food-related reward sensitivity (Schag et al., 2013; Schmidt et al., 2016; Sperling et al., 2017). Given that weight-matched controls without BED did not show these difficulties, it is unlikely that increased inhibition errors are merely a consequence of overweight/obesity. Difficulties in inhibitory control, a component of impulsivity, are likely to facilitate binge-eating behavior, therefore maintaining core psychopathology of the disorder (Balodis, Grilo, & Potenza, 2015). The lack of group differences between those with NES and HCs suggests different attentional processes area associated with NES and BED (Baldofski et al., 2018). However, it is possible that the small sample size in the NES group (n = 19), especially when only full-syndrome cases were considered (n = 12), resulted in insufficient power to detect group differences. Larger studies in both BED and NES are required.

There was evidence that individuals with AN or BED process images of their own body differently from the bodies of others, as opposed to having a general bias towards body related stimuli (Svaldi et al., 2012). However, due to the diverse range of methodologies used in these studies, findings were mixed. For example, Blechert et al. (2010) used a dot-probe paradigm, finding that participants with AN showed an attentional bias towards photographs of their own bodies, whereas those with BN and HC did not. However, another study reported no differences in viewing times between those with AN, BN, clinical controls, or HCs—all groups looked at their own bodies for more time than other bodies (Bauer, Schneider, Waldorf, Braks, et al., 2017). The dot-probe paradigm taps into covert attention when self and other bodies are competing, and may reflect an automatic, pre-intentional bias. These subtle differences may have been missed in the latter study, which measured looking times when photographs were presented alone.

Generally, AN, BN, and BED displayed an attentional bias for parts of their body they deemed unattractive, a pattern which was weaker or not present in HC (Freeman et al., 1991; Svaldi et al., 2011; Svaldi et al., 2016; Tuschen-Caffier et al., 2015). Again, in those with AN, this bias seems to be automatic (Bauer, Schneider, Waldorf, Cordes, et al., 2017). Cognitive theories of body dissatisfaction propose that schemas related to body image give rise to a number of cognitive biases affecting attention, memory, interpretation, and judgement. These selective cognitive processes lead to negative emotions regarding body image, and further reinforce negative schemas (Rodgers & DuBois, 2016). Indeed, several studies included here reported that the more dissatisfied participants were with their body, the stronger their attentional bias was (Bauer, Schneider, Waldorf, Braks, et al., 2017; Blechert et al., 2010; Svaldi et al., 2012; Svaldi et al., 2016; Tuschen-Caffier et al., 2015). This effect has been reported in non-clinical populations (Rodgers & DuBois, 2016), and generally was not specific to those with EDs in the studies included here.

These findings regarding body-related attention may have implications for treatment. Attentional bias modification treatment (ABMT) aims to implicitly retrain early attentional processes away from threatening/emotional stimuli, and has been used successfully in anxiety disorders (Hakamata et al., 2010; Heeren, Reese, McNally, & Philippot, 2012). ABMT has also shown promise in reducing negative interpretation biases for social stimuli in individuals with AN (Cardi et al., 2015; Turton, Cardi, Treasure, & Hirsch, 2017), and reducing ED symptoms in those with BED (Boutelle, Monreal, Strong, & Amir, 2016; Schmitz & Svaldi, 2017). While mirror exposure is often used in enhanced cognitive behavioral therapy (CBT-E) for EDs, such techniques involve conscious reappraisal and gradual extinction of the negative affective response towards ones body (Fairburn et al., 2008), rather than directly manipulating subcortical attentional processes (Renwick et al., 2013). ABMT for body image bias has yet to be explored in clinical ED samples.

Individuals with AN and AN-WR looked at different areas of the body when making judgments about attractiveness and body size, compared to HCs (Cornelissen et al., 2016; George et al., 2011). The pattern of fixations displayed by HCs (concentrated on the waist and stomach area) was consistent with an efficient sampling strategy, given these areas are a good index of overall BMI (Cornelissen, Toveé, & Bateson, 2009). However, when stimuli were point-light walkers, fixation patterns and body size judgements did not differ between those with AN and HC (Phillipou, Rossell, Gurvich, Castle, et al., 2016). The differing results are likely due to the use of biological motion stimuli, which are devoid of information about the surface level shape of the body. Thus, it seems that overestimation of body size, a key characteristic of AN, is based on different sampling of the body size information available. Techniques that reveal this discrepancy may be helpful as part of an intervention to improve body image disturbance in AN. Although body image disturbance is considered a particularly difficult symptom to treat, new experimental methods such as virtual reality have provided promising results, demonstrating

that body size judgments can be changed (Keizer, van Elburg, Helms, & Dijkerman, 2016).

Eye-movement patterns in participants with AN showed some similarities to those found in anxiety disorders. For example, individuals with AN had a stronger initial tendency to orient to food stimuli, but looked at food for less time overall than HC (Giel et al., 2011). This is consistent with vigilance-avoidance theory; a pattern of attention characterized by early attention to, and subsequent avoidance of a fear-relevant stimulus. Such patterns of attention have been demonstrated in those with social anxiety (Garner, Mogg, & Bradley, 2006; Vassilopoulos, 2005) and spider phobia (Pflugshaupt et al., 2005; Rinck & Becker, 2006). Early vigilance towards one's own body compared to other body stimuli was also demonstrated, and towards unattractive areas of one's own body (Blechert et al., 2010; Phillipou, Rossell, Gurvich, Hughes, et al., 2016). These findings suggest an automatic, pre-cognitive bias for food and body stimuli in those with AN, possibly reflecting the aversive nature of these stimuli. There was also evidence for "hyper-scanning" of biological motion stimuli and faces in AN, a behavior thought to reflect increased vigilance due to anxiety (Phillipou et al., 2015; Phillipou, Rossell, Gurvich, Castle, et al., 2016). However, only one study included a measure of anxiety (Blechert et al., 2010), but did not examine its association with eye-movements. Including measures of comorbid traits such as anxiety may be important in determining factors that contribute to attentional biases in EDs.

Relatedly, similarities between AN and other psychiatric disorders were found in smooth pursuit and saccadic eye-movement parameters. Lower pursuit gain reported in those with AN-WR (Pallanti et al., 1998) has been found in those with schizophrenia, depression (Kathmann, Hochrein, Uwer, & Bondy, 2003; O'Driscoll & Callahan, 2008; Tien, Ross, Pearlson, & Strauss, 1996), and OCD (Pallanti et al., 1996). Commenting on the similarities with OCD, Pallanti et al. (1998) suggest that the obsessional and perfectionistic traits in AN may reflect a behavioral expression of a shared underlying biological vulnerability. Increased rates of inhibitory errors on a memory guided saccade task were also reported in those with AN (Phillipou, Rossell, Gurvich, Hughes, et al., 2016), a finding that has again been reported in OCD (Rosenberg, Dick, O'Hearn, & Sweeney, 1997). To explore whether eye movement abnormalities are state or trait markers in AN and other EDs, it would be of interest to examine whether performance on smooth pursuit and saccade measures are related to clinical improvements. In schizophrenia, eye-movement abnormalities improve alongside improvements in delusional symptoms, however they do not reach the level of HCs even in the remitted state (Beedie, Benson, & St Clair, 2011).

There is emerging evidence for avoidance of eyes and faces in those with AN, a finding that has also been demonstrated in non-clinical samples with high ED psychopathology (Sharpe, Wallis, & Ridout, 2016). Eye avoidance was also found in AN-WR, suggesting independence from clinical improvements (Watson et al., 2010). Avoidance of the eyes and social stimuli has been reported in ASD, and is considered a key characteristic of the disorder (Black et al., 2017). Interestingly, AN and ASD show a range of similarities in symptoms, including difficulties in theory of mind (Leppanen, Sedgewick, Treasure, & Tchanturia, 2018), emotion recognition (Bal et al., 2010; Kucharska-Pietura, Nikolaou, Masiak, & Treasure, 2004; Kuusikko et al., 2009) and production (Davies et al., 2016; McIntosh, Reichmann-Decker, Winkielman, & Wilbarger, 2006), high levels of alexithymia (Bird & Cook, 2013; Westwood, Kerr-Gaffney, Stahl, & Tchanturia, 2017) and social anxiety (Kerr-Gaffney, Harrison, & Tchanturia, 2018; Simonoff et al., 2008). Around 10% of those with AN meet diagnostic criteria for ASD, while a further 40% show high levels of ASD symptoms (Westwood, Mandy, Simic, & Tchanturia, 2018). To understand possible mechanisms behind the eye movement patterns associated with AN, it may be useful to investigate their associations with comorbid psychopathology, such as ASD or social anxiety. For example, the eye avoidance hypothesis proposes that there is hyper-arousal of the amygdala in response to social stimuli in ASD. As a result, individuals direct their attention away from the eyes to regulate their arousal and perceived threat (Corden et al., 2008; Tanaka & Sung, 2016).

Several methodological limitations are apparent across studies. For example, only three studies controlled for the effects of psychotropic medication on eye-movements (Fujiwara et al., 2017; Giel et al., 2011, 2013), while a further three only included participants who were medication free (Baldofski et al., 2018; Pallanti et al., 1998; Sperling et al., 2017). Atypical antipsychotics and benzodiazepines have been found to reduce saccadic velocity and increase latency in healthy individuals, due to their sedative effect on the central nervous system (Reilly, Lencer, Bishop, Keedy, & Sweeney, 2008). Although the results of the studies included in this review did not generally differ when medication was controlled for, most did not report on medication status. Given that atypical antipsychotics are increasingly being used to treat those with AN (McKnight & Park, 2010), this is an important methodological consideration for future eye-tracking research.

Relatedly, few studies reported on associations between eye movements and clinical variables such as BMI, illness duration, or ED psychopathology. Such factors may be important given the neural, cognitive, and low-level motor impairments that occur with malnutrition in AN (Joos et al., 2010; King et al., 2015; Titova et al., 2013; Zakzanis et al., 2010). Indeed, in the few studies that did report associations with clinical variables, higher BMI and ED psychopathology in those with BED or NES was found to be associated with shorter gaze duration to food stimuli (Baldofski et al., 2018; Schmidt et al., 2016). This pattern may reflect attentional avoidance or disengagement strategies being employed by those with more severe ED psychopathology. Such strategies may be dysfunctional, as they may interfere with habituation to food stimuli, thus resulting in more binge-eating episodes and associated weight gain (Epstein, Leddy, Temple, & Faith, 2007; Epstein, Robinson, Roemmich, & Marusewski, 2011). Interestingly, shorter gaze duration to food was associated with higher ED psychopathology and lower BMI in participants with AN (Giel et al., 2011), perhaps illustrating a cycle observed clinically, whereby avoidance of food and further restriction increases ED cognitions. Given these findings, future eye-tracking research in EDs should consider the effect of state variables on eye movement patterns and attentional biases.

Another limitation is that many different outcome measures were used across studies, however the rationale for using one over the other was not always clear. The lack of standardization of

outcome measures may have influenced the way in which the results were reported. Similarly, variations in stimuli and presentation times make comparisons across studies difficult. For example, when examining attention to body parts, a few studies did not exclude the head/face from the body stimuli (Cornelissen et al., 2016; Freeman et al., 1991; Svaldi et al., 2016; Tuschen-Caffier et al., 2015; Von Wietersheim et al., 2012). Since faces are highly salient to humans (Bindemann, Burton, Hooge, Jenkins, & de Haan, 2005; Theeuwes & Van der Stigchel, 2006), their inclusion is likely to affect attention considerably, thus introducing a potential confound and making comparisons across studies difficult. On the other hand, body stimuli that include faces are likely to better represent visual stimuli encountered in everyday life.

In addition, different types of eye trackers, with different spatial and temporal resolutions will affect the accuracy of the results. Most studies used a tracker that required the head to be held stable using a chin rest, which, while perhaps providing better spatial accuracy, suffers from a lack of ecological validity (Niehorster, Cornelissen, Holmqvist, Hooge, & Hessels, 2018). Remote view eye-trackers, which do not restrict head movements, were also used in several studies. It is proposed that such techniques provide a more natural assessment of eye gaze, however they have been found to suffer from considerable data loss and reduced sampling rates when participants heads are in non-optimal orientations (Niehorster et al., 2018). Despite these limitations, some innovative techniques were demonstrated, for example using head mounted eye-tracking devices to measure gaze towards participants' own image in a mirror (Svaldi et al., 2016; Tuschen-Caffier et al., 2015). This technique is particularly fitted to ED populations, given the body checking behaviors often seen in this group. Nonetheless, there is a need for studies to follow a standardized methodological approach for investigating eye movements to substantiate some of the findings included in this review. For example, protocols have been developed for studying saccadic eye-movements in order to improve reproducibility (Nij Bivjank et al., 2018). This would also be helpful in making comparisons across psychiatric disorders (Bittencourt et al., 2013; Rommelse, Van der Stigchel, & Sergeant, 2008).

To conclude, a variety of interesting paradigms have been used in eye-tracking research in EDs, however replications and more consistent use of specific outcome measures and tasks are required. Attentional biases towards food and body stimuli in those with EDs may represent an important target for treatment, for example using ABMT. Emerging evidence suggests there are also differences in the way those with AN attend to social information, and future studies should utilize the paradigms that have been established in disorders such as ASD. If social information is not attended to, social cues that are key to successful interactions are likely to be missed, making it difficult to build relationships. This is important, given that interpersonal difficulties are associated with poorer treatment outcomes in EDs (Jones, Lindekilde, Lübeck, & Clausen, 2015; Vall & Wade, 2015). Further, the saccadic abnormalities found in those with AN should be investigated in other EDs, in order to examine possible alterations in neuronal circuits responsible for ocular motor control.

ACKNOWLEDGMENTS

J.K.G. is supported by the Economic and Social Research Council (ESRC). K.T. would like to acknowledge financial support from MRC and MRF Child and Young Adult Mental Health—the underpinning etiology of self-harm and eating disorders.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Kerr-Gaffney J, Harrison A, Tchanturia K. Eye-tracking research in eating disorders: A systematic review. *Int J Eat Disord*. 2018;1–25. https://doi.org/10.1002/eat.22998

Since the publication of this review, two further eye-tracking studies examining social attention in AN have been published. Harrison et al. (2019) examined attention to eyes during viewing of (a) static faces displaying basic emotions, (b) videos of two actors conversing, and (c) a real-life social interaction with the researcher in individuals with AN, recovered AN, and HCs. Those with AN looked at the eyes less often and for a shorter duration than HCs in all three conditions. The recovered AN group showed an intermediate profile; attending to the eyes more frequently than acute AN but less frequently than HCs across all conditions. Further, a shorter duration of eye contact during the social interaction was significantly associated with higher levels of social anhedonia, work and social adjustment difficulties, and the number of close friends in individuals with AN. Although correlational, this finding is important as it indicates there may be a relationship between social attention and real-life social functioning in AN. In the second study, attention to static face images was recorded while participants recovered from AN and HCs engaged in an emotion recognition task (Dinkler et al., 2019). There were no significant differences in attention allocation between groups. The differing results in recovered AN reported in these studies might be due to differences in the number of years participants had been recovered – participants in the former study had been recovered for a mean of 3.2 years, whereas those in the latter study represented a long-term recovered group (80% had been recovered for at least 12 years). Different from the results of a previous study (Fujiwara et al., 2017), Dinkler and colleagues found that emotion recognition accuracy was not associated with attention to the eye region. This might suggest attentional processes underlying emotion recognition differ in acute and recovered AN.

1.5.2 Perception of nonverbal communication

A considerable amount of communication occurs through nonverbal channels, with gesture, facial expression, and actions conveying information about an individual's thoughts, emotions, and mental states. Understanding these nonverbal communicative cues is vital for successful social interaction, as the perceiver acquires information helpful for guiding the interaction and their own behaviour (Johnston et

al., 2008; Lazarus, 1991; Patterson, 2019). Difficulties in this area have been observed in individuals with AN, potentially contributing to the interpersonal problems associated with the disorder.

Most studies examining perception of nonverbal communication in individuals with AN have investigated facial emotion recognition abilities. A meta-analysis of studies in this domain showed that individuals with AN were poorer at recognising emotions relative to HCs, with a small to medium effect size for basic emotions and a large effect size for complex emotions (Oldershaw et al., 2011). Two studies included in the review also measured emotion recognition in those recovered from AN, both using the Reading the Mind in the Eyes Task (Baron-Cohen, Wheelwright, Hill, et al., 2001). Harrison, Tchanturia, and Treasure (2010) found that AN and recovered AN scored significantly lower than HCs (with no significant difference in performance between the AN groups), while Oldershaw et al. (2010) found that emotion recognition did not significantly differ across the three groups. Interestingly, several studies have demonstrated that emotion recognition performance may differ depending on the valance of the emotions displayed; with those with AN showing poorer performance for negative emotions only (Castro et al., 2010; Kucharska-Pietura et al., 2004; Oldershaw et al., 2010). This finding might be due to individuals with AN paying less attention to negative emotional faces. Indeed, a recent eye-tracking study showed that difficulties recognising anger and disgust in a mixed ED group (AN and BN) were predicted by less visual attention to faces, particularly the eye region (Fujiwara et al., 2017).

Studies using facial emotion recognition tasks have somewhat limited ecological validity. Stimuli are static images restricted to the face or eye region, without the tone of voice, body language, or contextual information that is inherent in everyday social situations. Some research has therefore investigated emotion recognition using different modalities of nonverbal communication in order to better understand social cognition in AN. For example, a few studies have investigated emotion recognition from body language using point light walker stimuli, which represent human movement through several points in place of the major joints of the body (Thompson & Baccus, 2012). Individuals with AN were less accurate at recognising

sadness compared to HC and weight-restored AN, but better at recognising anger (Lang et al., 2015; Zucker et al., 2013). However, in one study, group differences became nonsignificant when BMI was controlled for in analyses, indicating that the degree of starvation associated with the acutely ill state might account for differences in emotion perception (Zucker et al., 2013). Thus, from the limited research available, it appears that individuals with AN may be poorer at recognising sadness from body movements. However, it is not known whether these difficulties extend to body language or gestures expressed by more ecologically valid human displays.

Perception of emotion through voice has also been examined in individuals with AN. Participants with AN were found to be significantly poorer at recognising both positive and negative emotions conveyed through spoken sentences relative to HCs (Kucharska-Pietura et al., 2004). However, after adjusting for covariates (age, education, current mood, and severity of depression), group differences became nonsignificant. Similarly, Oldershaw et al. (2010) found that adults with AN were significantly poorer at recognising positive and negative emotions compared to both HC and recovered AN. Clinical variables (BMI, illness duration, age of onset, severity of anxiety and depression, and ED psychopathology) were not related to emotion recognition performance. Thus, while there may be difficulties in recognising emotions from voice in AN, evidence is mixed as to whether this is due to the illness itself or other clinical or demographic variables. Importantly, the only comorbid disorders assessed in these studies were anxiety and depression. Given that AN often occurs with high levels of ASD traits (Westwood & Tchanturia, 2017), including such measures may be useful in further understanding possible relations between social cognition and comorbid psychopathology.

Other research has examined perception of nonverbal behaviour more holistically, using paradigms that include facial expression, posture, body movements, and vocal prosody together. In one study, participants viewed videos of an interviewer giving critical feedback, and rated the actor on perceived dominance/submissive and warmth/coldness (Ambwani et al., 2016). Nonverbal cues included eye gaze, head tilt, posture, and use of bodily space. Participants with AN rated the actors as significantly less warm than HCs, a difference which remained after controlling for

levels of depression, anxiety, and stress. However, the videos also included verbal statements by the actor (e.g., “you did an excellent job”), therefore the task was not purely a measure of nonverbal behaviour. Similarly, Brockmeyer et al. (2016) used the Movie for Assessment of Social Cognition (Dziobek et al., 2006), in which participants view clips of social situations involving complex ToM, conveyed through both verbal and nonverbal expressions (facial expressions, body language, gestures) of thoughts and emotions. Participants with AN performed similarly to HCs in understanding cognitive mental states (e.g., “What is this person thinking/intending?”) but were significantly worse at understanding emotional ones (e.g., “What is this person feeling?”). Performance was unrelated to BMI, duration of illness, and levels of ED psychopathology, depression, and anxiety. Again, since the clips involved speech, it is not known whether difficulties in perception of nonverbal cues were responsible for the reduced understanding of mental states.

To our knowledge, only one study has addressed this issue, examining perception of nonverbal communication through different modalities in AN without accompanying verbal information. Bentz et al. (2017) used the Mini Profile of Nonverbal Sensitivity (MiniPONS; Bänziger et al., 2011) in individuals with first-episode AN, recovered AN, and HCs. The MiniPONS comprises a series of clips, with an actor conveying emotions and intentions through several aspects of nonverbal communication. Importantly, the different clips allow different modes of nonverbal communication to be studied systematically (face only, body only, voice only, face and voice together). Interestingly, recovered participants performed significantly worse on body only and voice only clips, compared to first-episode AN and HCs, who did not differ from one another. The authors suggest this might be due to the lower age of illness onset in the recovered AN group; such that the illness may have impeded a critical window of development of social perception skills.

1.5.3 Empathy

Another possible mechanism that might underlie interpersonal difficulties in AN is empathy. Empathy is considered a key component of social cognition, cooperation, and prosocial behaviour, as it allows us to make sense of and respond appropriately

to other people's behaviour (Decety et al., 2016; Eisenberg & Miller, 1987). It comprises two major facets: cognitive and affective empathy. Cognitive empathy refers to the ability to recognise and understand another's mental state (part of ToM or "mentalising") while affective empathy is the ability to share the feelings of others, without any direct emotional stimulation to oneself. These two aspects of empathy rely on different brain structures and take different developmental pathways, with affective empathy developing much earlier than cognitive empathy (Singer, 2006).

Interest in empathy in AN began with a longitudinal study by Gillberg et al. (1994). Participants with adolescent-onset AN were compared with sex- and age-matched controls on various outcome measures 5 years after the original diagnostic study (Gillberg & Råstam, 1992). The authors report that a subgroup of participants with AN met criteria for an "empathy disorder"; those with severe problems in social understanding and communication, consistent with a diagnosis of ASD. Poorer outcomes in terms of recovery and psychosocial functioning were found in this group 18 years after illness onset (Anckarsäter et al., 2012; Wentz et al., 2009). Since then, several studies have used self-report measures, such as the Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004) and the Interpersonal Reactivity Index (IRI; Davis, 1983) to explore empathy in individuals with AN. Results from these studies are mixed; with some studies reporting significantly lower levels of empathy in individuals with AN compared to HCs (Adenzato et al., 2012; Jermakow & Brzezicka, 2016; Morris et al., 2014), and others reporting no differences (Courty et al., 2013; Hambrook et al., 2008; Lulé et al., 2014). Further, few self-report studies distinguish between cognitive and affective empathy, a distinction that has been shown to be important in disorders such as ASD (Mazza et al., 2014) and schizophrenia (Michaels et al., 2014).

Very few studies have examined actual empathic performance in individuals with AN. Cardi et al. (2015) asked participants to rate the intensity of their emotions while watching video clips depicting an individual displaying either happiness, sadness, anger, or a neutral expression. No significant differences were found between ED (AN or BN) and HC groups. Brewer et al. (2019) used an empathy for pain paradigm, whereby ED and HC participants were shown a series of painful or non-painful

pictures, and asked to recall whether the picture depicted a right or left hand or foot. The difference in RTs between painful and non-painful trials was taken as an "empathic interference effect". Again, there was no difference between ED (AN or BN) and HC groups. Instead, high levels of alexithymia were associated with increased empathy, an association that has also been found in self-report studies (Adenzato et al., 2012). Given that socio-emotional abilities in AN and BN often differ (Bora & Kose, 2016), the lack of group differences may be due to the mixed ED samples used in both studies. Importantly, the latter study demonstrates that comorbid traits such as alexithymia may explain differences in emotion processing, rather than the ED itself.

1.5.4 Relationships between comorbid symptoms and social cognition in AN

While many studies have examined the effects of anxiety and depression symptoms on social cognition in AN, results are inconsistent (Cardi et al., 2012; Fujiwara et al., 2017; Harrison, Tchanturia, & Treasure, 2010; Jänsch et al., 2009; Oldershaw et al., 2010; Pollatos et al., 2008). Further, the vast majority of studies have only included correlational analyses, limiting interpretation of any associations found. Most importantly, very few studies have included measures of ASD symptoms, which are highly relevant given their high co-occurrence with AN, and the socio-emotional alterations associated with ASD. Indeed, many of the socio-emotional difficulties discussed here in individuals with AN are considered core characteristics of ASD. For example, research has consistently demonstrated reduced attention to social information, and especially eyes, in individuals with ASD (Chita-Tegmark, 2016). Delayed orienting to faces in particular has been identified as one of the earliest and most basic social impairments in individuals with ASD, and may contribute to difficulties in social communication later in life (Dawson et al., 1998). Similarly, impairments in ToM, emotion recognition, and empathy are well documented in individuals with ASD (Baron-Cohen & Wheelwright, 2004; Bons et al., 2013; Griffiths et al., 2019; Loth et al., 2018; Rigby et al., 2018).

Studying the impact of ASD traits on social cognition in individuals with AN is important for a number of reasons. Firstly, it is possible that variations in ASD

symptoms across study samples may in part explain the mixed results regarding emotion recognition, empathy, and social attention in AN. In samples with relatively few individuals with AN and high ASD traits, analyses of group differences may not reveal difficulties in socio-cognitive domains compared to HCs. However, significant group differences may emerge in samples with higher levels of ASD traits and therefore more difficulties in socio-emotional cognition. Following this reasoning, Renwick et al. (2015) used hierarchical cluster analysis to characterise heterogeneity in neuro- and socio-cognitive performance in individuals with AN. Three clusters emerged: one with overall average to high neuro- and socio-cognitive performance, one showing mixed performance, and a third with distinct weaknesses in central coherence, set shifting, and theory of mind. This third ASD-like cluster made up 17% of the sample. This study demonstrates that by solely focussing on mean between-group differences, relatively severe difficulties in small sub-samples of individuals with AN may be missed. Further, difficulties in these domains could constitute stratification biomarkers; characteristics that vary between subgroups of individuals with AN, reflecting differences in aetiological mechanisms, symptom presentation, and/or treatment responses (Loth et al., 2016).

Relatedly, studying overlap in socio-emotional cognition in individuals with AN and those with ASD may lead to new insights into underlying mechanisms. For example, reduced attention to the eyes has been found to predict degree of impairment in emotion recognition abilities, as well as lower social competence in those with ASD (Corden et al., 2008; Falkmer et al., 2011; Klin et al., 2002; Müller et al., 2016). It is therefore possible that a similar mechanism might underlie emotion recognition difficulties in AN. It is hoped that understanding overlap in underlying social-cognitive mechanisms between AN and other disorders may help to define behavioural endophenotypes beyond current diagnostic classification systems. This may lead to a greater understanding of the aetiology of AN, and generate new ideas for treatment.

1.6 Aims and hypotheses

The overall aim of the thesis is to investigate the impact of ASD symptoms on socio-emotional cognition in adults in the acute and recovered stages of AN, compared to

HCs. The overarching hypotheses stated that (a) ASD symptoms would be significantly elevated in both acute and recovered AN, compared to HCs, and (b) the presence of ASD symptoms would be associated with difficulties in socio-emotional cognition. Given that AN also commonly co-occurs with anxiety, depression, and alexithymia, we also included quantitative measurements of these comorbidities in order to provide a full assessment of the impact of comorbidities on socio-emotional cognition. The thesis is presented as a series of studies, with separate aims and hypotheses, as outlined below. The first few studies focus on exploring comorbid ASD symptoms in AN, while the latter part of the thesis examines performance in a variety of socio-cognitive domains.

Study 1 - The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa

Study 1 is a cross-sectional study examining associations between scores on self-report and observational clinical interview measures of ASD symptoms in individuals with AN. Despite being widely used in ASD research, this is the first study to use the Social-Responsiveness Scale, adult self-report version (SRS-2; Constantino & Gruber, 2012) in individuals with AN. Given that the SRS-2 would be used in later studies included in the thesis, this study provided important information on its utility as a measure of ASD traits in individuals with AN.

Aims: the study aimed to examine (a) group differences on the SRS-2 in individuals in the acute and recovered stages of AN, compared to HCs, (b) associations between scores on the SRS-2 and the ADOS-2, (c) associations between SRS-2 scores, ED severity, and functional impairment.

Study 2 - Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach

Although accumulating evidence suggests a relationship between AN and ASD, the nature of this comorbidity is unclear. Study 2 is the first study to map relationships

between ED and ASD symptoms in individuals with AN using a network analytic approach, in order to understand which symptoms are most strongly connected to symptoms of the other disorder.

Aims: (a) to examine relationships between ED and ASD symptoms in individuals with a lifetime history of AN using network analysis, (b) to identify central nodes in the network (c), to identify bridge nodes in the network.

Study 3 – Self-reported autistic traits mediate reductions in social attention in adults with anorexia nervosa

Study 3 is a cross-sectional study examining patterns of attention during viewing of a dynamic social scene using eye-tracking.

Aims: the study aimed to examine (a) group differences in attention to faces, as well as core facial features (eyes, nose, mouth), while viewing a naturalistic, dynamic social scene in individuals with AN, REC, and HCs, and (b) whether comorbid psychopathology (ASD, alexithymia, depression, anxiety, and social anxiety) was associated with social attention.

Hypotheses: It was predicted that (a) individuals with AN would spend less time looking at faces and eyes of faces compared to HCs, while REC would show intermediate levels of attention, and (b) high levels of ASD traits would be associated with less time spent looking at faces and eyes, as well as a longer delay until first fixation on the face.

Study 4 - Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits

Study 4 is a cross-sectional study examining facial emotion recognition performance. The study also used eye-tracking to measure attention to faces during emotion recognition.

Aims: the study aimed to investigate (a) group differences in basic and complex facial emotion recognition performance in individuals with AN, REC, and HCs, (b) whether

visual attention to faces predicted emotion recognition performance, and (c) whether levels of comorbid psychopathology (ASD, alexithymia, depression, anxiety, and social anxiety) were associated with emotion recognition performance.

Study 5 - Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis

Although several reviews have examined emotion recognition and ToM performance in individuals with AN, empathy has received little attention. In order to synthesise the mixed literature on empathy in AN, study 5 provided a systematic review and meta-analysis of self-reported empathic abilities in individuals with EDs. Although all EDs were included, the majority of studies examined individuals with AN.

Aims: to examine (a) differences in both cognitive and affective empathy in individuals with EDs compared to HCs, and (b) associations between empathy, psychopathology, and clinical variables.

Study 6 - Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa

Study 6 is a cross-sectional study examining group differences across two aspects of socio-emotional cognition; empathy and perception of nonverbal communication. This study is the first to use a performance-based measure of both cognitive and affective empathy in individuals with AN. In addition, perception of nonverbal communication was measured by systematically manipulating different nonverbal modalities for comparable stimuli, allowing for differences in the ability to use different nonverbal cues to be examined.

Aims: to examine (a) cognitive and affective empathy and perception of nonverbal communication in individuals with AN, recovered AN (REC), and HCs, using performance-based measures, and (b) potential relationships between comorbid psychopathological traits (ASD, alexithymia, depression, anxiety, and social anxiety) and performance on social cognition tasks.

Hypotheses: individuals with AN were predicted to display poorer cognitive empathy performance compared to HCs. Scores in the REC group were predicted to be higher than AN but lower than that of HCs. Affective empathy performance was hypothesized to be similar across groups. Regarding perception of nonverbal communication, it was predicted that individuals with AN would show lower overall performance compared to HCs. Again, scores in the REC group were predicted to be higher than AN but lower than that of HCs.

Chapter 2 - Methods

The individual methods used in each study are presented within their respective manuscripts or chapters, however the general methods used throughout are described here in more detail. Given that analytic strategies varied considerably across studies, these are presented in manuscripts or chapters only.

2.1 Design

Studies 1, 3, 4, and 6 used a cross-sectional design, with three groups: acute anorexia nervosa (AN), recovered AN (REC), and healthy controls (HCs). The groups were matched for age, sex, and IQ. Study 2 also used a cross-sectional design, consisting of participants with a lifetime diagnosis of AN only (AN and REC). Study 5 used a meta-analytic design and also included meta-regression.

2.2 Participants

2.2.1 Inclusion and exclusion criteria

Inclusion and exclusion criteria for participants in studies 1, 2, 3, 4, and 6 are shown in Table 1 (note that HCs were not included in study 2). The Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV; First et al., 2015) was used to confirm a past or current diagnosis of AN, and the absence of a current or past psychiatric disorder in HC participants (see Section 2.4.1.1).

Table 1. Inclusion and exclusion criteria for participants

AN	REC	HC
	Inclusion criteria	
Normal/corrected to normal vision	Normal/corrected to normal vision	Normal/corrected to normal vision
18 – 55 years old	18 – 55 years old	18 – 55 years old
Fluent in English	Fluent in English	Fluent in English
BMI ≤18.5	BMI 19 – 27 (and maintained in this range for at least one year)	BMI 19 - 27

Current AN diagnosis	Past AN diagnosis	EDE-Q score <2.7
	Exclusion criteria	
A history of brain trauma, neurological impairment, or serious learning disability	A history of brain trauma, neurological impairment, or serious learning disability	A history of brain trauma, neurological impairment, or serious learning disability Past or current psychiatric disorder

AN, anorexia nervosa; BMI, body mass index; EDE-Q, eating disorder examination questionnaire; HC, healthy control; REC, recovered anorexia nervosa

2.2.2 Recruitment

Participants were recruited from four sources:

- **Specialist adult eating disorder (ED) services**: notices for the study were displayed around inpatient and daypatient ED wards at the South London and Maudsley (SLaM) and Central North West London (CNWL) National Health Service (NHS) ED services. In addition, participant information sheets were distributed to patients during ward meetings. Outpatients were also recruited at SLaM through notices on display at the ED service, and through a monthly email sent to staff informing them of research studies open for recruitment. Only participants with current AN were recruited through specialist ED services.
- **Online advertisement**: advertisements for the study were posted on a UK ED charity website, Beat (https://www.beateatingdisorders.org.uk/), a UK mental health charity website, MQ (https://www.mqmentalhealth.org/), and a participant recruitment website (https://www.callforparticipants.com/). Both REC and AN participants were recruited through online advertisements.
- **King's College London (KCL)**: an advertisement for the study was posted in the college research circular email send to all staff and students. In addition, notices were displayed around campuses. Participants from all three groups were recruited through KCL.

- **ED research group participant database:** participants who had taken part in another study at the KCL ED research group and who had consented to be contacted about future research studies were invited to take part. Participants from all three groups were recruited from the database.

Participant recruitment figures for each source are presented in Table 2. One hundred and fifty-three participants were recruited in total.

Table 2. Participant recruitment figures

	AN	REC	HC
SLaM eating disorder service	16	-	-
CNWL eating disorder service	5	-	-
Online	11	25	-
King's College London	3	19	47
Participant database	16	7	4
Total	51	51	51

AN, anorexia nervosa; CNWL, Central North West London; HC, healthy control; REC, recovered anorexia nervosa; SLaM, South London and Maudsley

2.3 Ethical approval

Ethical approval was granted by the London Camberwell St Giles NHS Research Ethics Committee (reference: 17/LO/1960). The study was also approved by the local research and design offices of the individual NHS trust recruitment sites. Written informed consent was obtained from all participants.

2.4 Measures

2.4.1 Demographic and clinical measures

2.4.1.1 Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV; First et al., 2015)

The SCID-5-RV is a semi-structured interview designed to identify a range of psychiatric disorders, including anxiety, depression, psychosis, attention deficit hyperactivity disorder, and EDs. It is widely used in psychiatric research protocols to identify past and current psychiatric symptoms for screening or participant selection purposes. The core screening questionnaire was used to screen for the presence of psychiatric symptoms in HCs, and those that screened positive were excluded from the study. Module I "Feeding and Eating Disorders" was used to confirm a current or past diagnosis of AN. AN and REC participants that did not meet criteria for a current or past diagnosis of AN were excluded.

2.4.1.2 Body mass index (BMI)

Height and weight were measured on the day of testing to calculate BMI (kg/m^2). Participants could be blind weighed if they wished. BMI was used to ensure participants met inclusion criteria (those that did not were excluded from analyses) and as an index of illness severity in the AN group.

2.4.1.3 Demographic questionnaire

All participants completed a demographic questionnaire which included questions regarding: age, ethnicity, medication use, employment, level of education, and marital status. In addition, participants in the AN and REC groups provided information regarding any treatment they were or had received and how old they were when they were first diagnosed with AN. Age at diagnosis was used to calculate illness length, another index of ED severity.

2.4.1.4 Wechsler Abbreviated Scale of Intelligence – 2nd edition (WASI-II; Wechsler, 2011)

Since individuals with AN demonstrate above average intelligence (Lopez et al., 2010), IQ was measured using the WASI-II to ensure the groups were similar in this respect. The WASI-II measures both verbal intelligence and perceptual reasoning, as well as full-scale IQ.

2.4.1.5 Autism Diagnostic Observation Schedule – 2nd edition (ADOS-2), module 4 (Lord et al., 2012)

The ADOS-2 is a standardised and widely used semi-structured observational interview for the assessment of ASD. Module 4 is for use with verbally fluent adolescents and adults. The interview includes a range of questions and activities designed to evoke behaviours and cognitions associated with ASD, and these are then scored on a scale of 0 to 3, with higher scores indicating more autistic behaviour. Interviews are typically video-recorded to aid with coding. The ADOS-2 covers four domains: language and communication, reciprocal social interaction, imagination, and stereotyped behaviours and restricted interests. The revised algorithm, which was designed to more closely reflect the DSM-5 criteria for ASD, was used for scoring (Hus & Lord, 2014). The algorithm comprises 15 items and has two subscales: social affect and restrictive and repetitive behaviours. Total scores of 8 or more indicate possible ASD. The revised algorithm demonstrates higher sensitivity and specificity than the original, especially for females (Hus & Lord, 2014; Pugliese et al., 2015), making it particularly suited to the current sample.

2.4.2 Socio-emotional processing measures

2.4.2.1 Naturalistic viewing of dynamic social scenes (Loth et al., 2017)

In study 3, eye movements were recorded during free viewing of a dynamic social scene to measure social attention. The stimulus was a movie clip from the dynamic images and eye movements database (“Fifty People One Question: Brooklyn”, http://thediemproject.wordpress.com/), in which several pedestrians in Brooklyn,

New York are interviewed and are seen speaking to the camera. The original audio accompanying the clip was replaced with background music, in order to control for the effects of speech comprehension on attention (Vo et al., 2012). The clip was chosen for its depiction of what would typically be seen when engaging in a natural social interaction, as well as its lack of body information (people were seen from the shoulders up), as this is known to be a salient class of stimuli in individuals with AN (Pinhas et al., 2014). The clip lasted 42s, and participants were asked to simply view the clip as they would watch television.

Total looking times (in seconds) to the screen were computed to control for overall attention to the stimulus, and total fixation duration to each area of interest (AOI) (whole face, eyes, nose, and mouth) was calculated (as a proportion of total valid samples). Dependent measures were: time spent looking at AOIs, time to first fixation on the face, and eye-to-mouth viewing ratio (fixation duration on eyes/fixation duration on eyes + fixation duration on mouth).

2.4.2.2 Films Expressions Task (FET; Garrido et al., 2009)

The FET is a facial emotion recognition task, modified to enable concurrent recording of eye movements. It has previously been used in individuals with ASD (Loth et al., 2018), however study 4 was the first to use the task in individuals with AN. In each trial, participants are first presented with an emotion word onscreen. Three images are then presented for 500ms each, one after another (with a 500ms blank screen between images). Images within each trial present the same actor displaying different emotional expressions. Participants are then asked to indicate, as quickly and as accurately as possible, which of the images displayed the emotion word by pressing the corresponding key (1, 2, or 3). There are 53 trials in total (preceded by 3 practice trials). Prior to the task, participants were presented with a sheet listing the target emotion words and their definitions to ensure they were familiar with the words. Images are from films made in non-English speaking countries to reduce the probability that participants would recognise the actors.

The task was chosen due to its depiction of naturalistic facial expressions; its inclusion of a range of both basic and complex emotions; and relatively brief presentation

times. Basic and complex emotion trials were presented interleaved, in a fixed random order. Foil emotional expressions were selected to be similar to the target emotion in terms of intensity of the expression and perceptual features. Dependent measures were accuracy (% of trials correct), mean reaction times (RTs), and time spent looking at the stimulus (as a proportion of presentation time).

2.4.2.3 Multifaceted Empathy Test (MET; Dziobek et al., 2008)

The MET is a performance-based measure of cognitive and affective empathy. It has been used in a number of populations, including individuals with ASD (Dziobek et al., 2008; Mazza et al., 2014), bipolar disorder (Bodnar & Rybakowski, 2017), and personality disorders (Dziobek et al., 2011; Rüter et al., 2010), however study 6 is the first to use the MET in individuals with AN. It was chosen for its realistic stimuli, which include a wide variety of complex emotional states alongside contextual information (e.g., a defeated woman in a hospital room). Stimuli are 40 photographs of people in various emotional states (20 positive and 20 negative), each presented twice. In 40 trials participants are asked to identify which emotion the person is feeling out of a choice of four emotions (cognitive empathy), and in a further 40 trials they are asked to indicate how much they empathise with the person depicted on a scale of 1 (*not at all*) to 9 (*a lot*) (affective empathy). Pictures were presented in a randomised order for each participant. Participants were asked to indicate their response by pressing the corresponding key as quickly and as accurately as possible, and pictures were displayed until a response was given. The MET was presented on a 14” PC monitor using Psychopy (Peirce, 2009).

The outcome measure for cognitive empathy is a total correct score out of 40, while affective empathy is a mean score ranging from 1 to 9. Positive and negative empathy scores were also calculated for affective and cognitive empathy. For all MET outcome measures, higher scores indicate higher levels of empathy.

2.4.2.4 Mini Profile of Nonberbal Sensitivity (MiniPONS; Bänziger et al., 2011)

The MiniPONS measures the ability to recognise emotions, communicative intentions, and interpersonal attitudes from different nonverbal modalities. It is a

short version of the 220 item Profile of Nonverbal Sensitivity, which has been validated in a number of populations (Rosenthal et al., 1979). Because the task systematically manipulates different nonverbal channels using comparable stimuli, it allows for differences in the ability to use different nonverbal cues to be examined. The task consists of 64 clips (2s each), depicting the same actor in different interpersonal situations. There are four different types of clip, representing different nonverbal modalities or combinations thereof: body only, face only, voice only (speech is either random-spliced or content-filtered in order to mask content but retain pitch and tone), and combined face and voice. Respondents are required to indicate the correct answer from a choice of two on a marking sheet after each clip. The MiniPONS was presented on a 14" PC monitor. Outcome measures were a total score out of 64, and scores out of 16 for each of the four channels.

2.4.3 Self-report measures

All self-report questionnaires are included in Appendix B.

2.4.3.1 Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994)

The EDE-Q measures severity of ED psychopathology, and is widely used as an outcome measure in clinical ED services and in research. It comprises 28 items, 22 of which are rated on a 7-point Likert scale (higher scores indicating more severe psychopathology). The scale also includes six items assessing frequency of various eating disorder behaviours, responses to which can take on any value and are not included in total score calculations. The EDE-Q has four subscales (eating concern, weight concern, shape concern, and restraint), and a global score (ranging from 0 to 6) is calculated by averaging responses across all items (excluding the six frequency items). The scale demonstrates good test-retest reliability and internal consistency, however empirical support for the original four factor structure is limited (Berg et al., 2012; Rand-Giovannetti et al., 2017).

Global scores were used as an index of ED symptom severity in studies 1, 3, 4, and 6, while individual items were used in the network analysis in study 2. In addition, a clinical cut-off score of ≥2.7 was used to ensure HCs with possible sub-threshold ED

symptoms were not included in analyses (Lang, Larsson, et al., 2016; Mond et al., 2004, 2006).

2.4.3.2 Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983)

The HADS is a 14-item questionnaire with two subscales measuring severity of anxiety and depression. Respondents are required to indicate on a 4-point Likert scale how they have been feeling in the past week, with higher scores indicating more severe symptoms. Subscale scores are interpreted as: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21). A total score out of 42 can also be calculated. Studies have consistently supported the two-factor structure of the HADS, and report good internal consistency and concurrent validity through high correlations with other measures of anxiety and depression (Bjelland et al., 2002).

2.4.3.3 Liebowitz Social Anxiety Scale, self-report version (LSAS; Liebowitz, 1987)

The LSAS measures severity of social anxiety symptoms, and has two subscales: fear and avoidance of social situations. It consists of 24 situations which are rated twice; once for severity of associated fear/anxiety and once for frequency of avoidance, yielding a total of 48 items. Answers are provided on a 4-point Likert scale, and are based on the respondent's experiences in the past week. A score of 60 out of a possible 144 has been established as a cut-off indicative of social anxiety disorder (SAD) (Rytwinski et al., 2009). The LSAS demonstrates good test-retest reliability, internal consistency, and convergent and discriminant validity (Baker et al., 2002; Heimberg et al., 1999). It is also sensitive to treatment change in individuals with SAD, and is recommended for outcome monitoring in clinical services (National Institute for Health [NICE], 2013).

2.4.3.4 Social Responsiveness Scale – 2nd edition, adult self-report form (SRS-2; Constantino & Gruber, 2012)

The SRS-2 measures symptoms associated with ASD, with higher scores indicating more autistic symptoms. The SRS-2 has 65 items, and five subscales: social awareness (ability to recognise social cues), social cognition (interpreting social behaviour),

social communication (reciprocal communication in social situations), social motivation (motivation to participate in social interactions), and restrictive interests and repetitive behaviour (circumscribed interests and stereotypy). Respondents indicate their agreement with each item on a 4-point Likert scale, rating their behaviour over the past six months. The sum of all items is calculated to provide a total score (max 195).

The SRS-2 has shown good psychometric properties in both clinical and non-clinical adult populations (Bölte, 2012; Takei et al., 2014). The original version is one of the most frequently used quantitative measures of ASD symptoms, however, no studies to date have used the measure in individuals with AN.

2.4.3.5 Twenty-item Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994)

The TAS-20 is a self-report measure of alexithymia. It has three subscales: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. Items are rated on a 5-point Likert scale, and total scores range from 0 to 100. Cut-off scores are established as follows: ≤51 = no alexithymia; 52-60 = borderline alexithymia; and ≥61 = alexithymia (Parker et al., 1993). The TAS-20 has good reliability and factorial validity in clinical and non-clinical samples (Loas et al., 2001; Taylor et al., 2003; Wise et al., 2000). It has also been used extensively in individuals with AN, and there is some evidence to suggest scores on the TAS-20 are associated with variations in socio-cognitive abilities in this population (Brewer et al., 2015; 2019; Westwood, Kerr-Gaffney, et al., 2017).

2.4.3.6 Work and Social Adjustment Scale (WSAS; Mundt et al., 2002)

The WSAS is a brief, 5-item measure of functional impairment. It assesses how the respondent's illness affects their functioning in five domains: work, home management, social leisure, private leisure, and ability to form and maintain close relationships. Scores range from 0 to 40, with a score of 20 or more indicating clinical significance. The WSAS has demonstrated good test-retest reliability and internal consistency, as well as being sensitive to treatment-related changes (Mundt et al., 2002). Previous research has shown that higher WSAS scores are associated with

more severe ED psychopathology and lower BMI in individuals with AN (Harrison et al., 2014; Tchanturia et al., 2013). The WSAS was used in studies 1, 3, 4, and 6 to examine whether ASD traits and socio-emotional cognition measures were associated with self-reported functional impairment.

2.5 Procedure

Participants attended a testing session at the Institute of Psychiatry, Psychology & Neuroscience (IoPPN). For 11 participants who were inpatients, testing was split over two sessions, with the eye-tracking tasks taking place at the IoPPN, and the rest of the tasks, questionnaires, and ADOS-2 interview taking place at their place of treatment. However, due to unforeseen circumstances (participants discharged from services, physical deterioration or medical complications prohibiting leave from hospital), five of these patients were unable to attend the eye-tracking session. As a result, these participants were not included in analyses in studies 3 and 4.

After written informed consent was obtained, the eye-tracking session began. Eye movements were recorded using a Tobii TX300 eye-tracker. The desktop mounted eye-tracker had a sampling rate of 300Hz, a screen resolution of 1920 x 1080, and a diagonal screen size of 23". Participants sat approximately 60cm from the screen. During tracking, infrared diodes generate reflections on the participant's retinas and corneas. From this reflection, the angular rotation of each eye is estimated. Before viewing the experimental stimuli (naturalistic scene followed by the FET), a 5-point calibration procedure ensured accuracy of gaze data for each participant. Calibration relates the angular rotation of each eye to the corresponding x and y coordinates on the screen surface. Stimuli presentation, behavioural data, and eye-tracking data were managed and recorded using custom written Matlab software (Mason, 2015, https://sites.google.com/site/taskenginedoc).

After eye-tracking, the researcher administered the WASI-II, the MET and the MiniPONS, and then conducted the ADOS-2. The participant then completed the questionnaires. At the end of the session, participants' heights and weights were

recorded. The session took around 2.5 hours, and participants were reimbursed £20 for their time.

Chapter 3 - The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa. *European Eating Disorders Review, 28*(4), 433-444. https://doi.org/10.1002/erv.2736

Received: 25 November 2019 | Revised: 9 March 2020 | Accepted: 16 March 2020

DOI: 10.1002/erv.2736

RESEARCH ARTICLE

WILEY

The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa

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Funding information
Economic and Social Research Council; Health Foundation , Grant/Award Number: 1115447; Medical Research Council, Grant/Award Number: MR/R004595/1; Psychiatry Research Trust; Swiss Anorexia Nervosa Foundation, Grant/Award Number: 58-16

Abstract

Objective: A significant proportion of individuals with anorexia nervosa (AN) show high levels of autism spectrum disorder (ASD) traits, a factor associated with poorer treatment outcomes. An important question for both researchers and clinicians relates to how ASD traits should be assessed in individuals with AN. This study aimed to examine scores on the Social Responsiveness Scale adult self-report version (SRS-2) in individuals in the acute (AN) and recovered stages (REC) of illness compared to healthy controls (HCs). We also aimed to examine associations between the SRS-2 and an observational diagnostic measure, the Autism Diagnostic Observation Schedule - second edition (ADOS-2).

Method: The SRS-2 and ADOS-2 were administered to 142 adults with AN, REC, and HCs. Eating disorder (ED) psychopathology and functional impairment were also assessed.

Results: AN and REC scored significantly higher than HCs on the SRS-2. SRS-2 scores significantly predicted ADOS-2 classification and were positively associated with ED psychopathology and functional impairment. SRS-2 scores were not associated with BMI or illness duration.

Conclusions: The SRS-2 may be a useful tool in screening for ASD traits in individuals with AN. Although cross-sectional, the results also suggest ASD symptoms are independent of BMI and persist in individuals recovered from AN.

KEYWORDS

anorexia nervosa, autism spectrum disorder, clinical interview, comorbidity, self-report

1 | INTRODUCTION

Over the past few decades, research has accumulated suggesting a relationship between anorexia nervosa (AN) and autism spectrum disorder (ASD). AN is a severe and potentially life-threatening eating disorder (ED) characterised by persistent restriction of energy intake and a disturbance in the way in which one's body weight or shape is experienced. In contrast, ASD is a neurodevelopmental disorder characterised by deficits in social communication and interaction and restrictive, repetitive patterns of behaviour or interests (American Psychiatric Association, 2013). While AN affects primarily females and typically develops in adolescence (Herpertz-Dahlmann, van Elburg, Castro-Fornieles, & Schmidt, 2015), ASD is more commonly diagnosed in males and symptoms are present from early childhood (Fombonne, 2009). Nonetheless, empirical research has documented a number of similarities in the phenotypic expressions of AN and ASD. In the neurocognitive domain, difficulties in set-shifting, weak central coherence, and superior attention to detail are seen in both individuals with AN and ASD (Happé & Booth, 2008; Jolliffe & Baron-Cohen, 1997; Lang, Lopez, Stahl, Tchanturia, & Treasure, 2014; Westwood, Stahl, Mandy, & Tchanturia, 2016), as well as their first-degree relatives (Bölte & Poustka, 2006; Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Tenconi et al., 2010; Wong, Maybery, Bishop, Maley, & Hallmayer, 2006). Regarding social-cognitive functioning, difficulties in theory of mind (ToM) and emotion recognition have been replicated extensively in individuals with ASD (Bal et al., 2010; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001; Happé, 1994; Kleinman, Marciano, & Ault, 2001; Kuusikko et al., 2009). Similarly, those with AN also show difficulties on ToM and facial emotion recognition tasks compared to healthy controls (HCs), although generally differences are of a smaller magnitude (Bora & Kose, 2016; Leppanen, Sedgewick, Treasure, & Tchanturia, 2018). Further, high levels of alexithymia and social anxiety are apparent in both disorders (Kerr-Gaffney, Harrison, & Tchanturia, 2018; Kinnaird, Stewart, & Tchanturia, 2019; Spain, Sin, Linder, McMahon, & Happé, 2018; Westwood, Kerr-Gaffney, Stahl, & Tchanturia, 2017).

Given these similarities, it is perhaps not surprising that between 4 and 52.5% of individuals with AN show clinically significant levels of ASD traits (Westwood & Tchanturia, 2017). This variation in part likely reflects differences in the tools used to assess ASD in those with AN. In order to provide a full diagnostic assessment of ASD, clinical guidelines recommend a formal assessment of current symptoms, using tools such as the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) as well as an assessment of early developmental history where possible (National Institute for Health and Clinical Excellence [NICE], 2012). However, this poses a problem for both researchers and clinicians; "gold standard" assessment tools such as the ADOS are lengthy, costly, and require extensive, ongoing training to administer. In addition, developmental history assessments such as the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) require an interview with an informant (e.g., a parent or guardian), which may be difficult to obtain from the families of adults with AN. Therefore, brief screening methods that aid identification of possible cases are required. Such measures should correlate with more comprehensive assessment tools in order to be useful. Further, measures that show agreement with measures of adaptive behaviour or functional impairment could provide useful information for treatment planning.

Several studies have used the Autism Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) or the abbreviated version (AQ-10; Allison, Auyeung, & Baron-Cohen, 2012) in individuals with AN, generally showing that those with AN score significantly higher than HCs (Westwood et al., 2016). The AQ is a 50 item self-report questionnaire assessing five domains: social skills; attention switching; attention to detail; communication; and imagination. In the original validation study, the AQ demonstrated reasonable face validity, with 80% of individuals with ASD scoring above the cut-off of 32, compared to 2% of HCs (Baron-Cohen et al., 2001). The AQ-10 has similar sensitivity and specificity to the full

Highlights

- Individuals in the acute and recovered stage of illness show higher levels of ASD traits than healthy controls on both self-report and clinical interview measures
- Score on the social responsiveness scale, adult self-report version (SRS-2) are associated with scores on the Autism Diagnostic Observation Schedule, second edition (ADOS-2), suggesting the SRS-2 may be useful screening tool for ASD in individuals with AN
- ASD traits were positively associated with severity of eating disorder psychopathology and functional impairment, but not BMI or illness duration

version, where a cut-off of 6 is recommended for screening purposes (Booth et al., 2013). However, there is some evidence to suggest that the AQ performs poorly in predicting an ASD diagnosis in adults with suspected ASD (Ketelaars et al., 2008). For example, in a large sample of adults referred to a national diagnostic service, Ashwood et al. (2016) reported that two-thirds of those scoring below the AQ cut-off were "false negatives" who did in fact have ASD (assessed using the ADOS and ADI-R). Neither version of the AQ correlated with ADOS scores, although weak correlations were found with the ADI-R. Further, "false positives" (those that scored above the AQ cut-off but did not receive a formal ASD diagnosis) were more likely to have comorbid general anxiety disorder, suggesting anxiety may inflate AQ scores. Only a few studies have examined associations between self-report ASD measures such as the AQ and scores on diagnostic interviews in individuals with AN. Generally, there is poor agreement between measures. Rhind et al. (2014) found that AQ-10 scores did not differ between adolescents with AN who were assigned an ASD diagnosis (using the Development and Well-being Assessment; Goodman, Ford, Richards, Gatward, & Meltzer, 2000) and those that did not. Sedgewick, Kerr-Gaffney, Leppanen, and Tchanturia (2019) found that AQ-10 scores were positively associated with ADOS-2 (Lord et al., 2012) scores in individuals recovered from AN but not in those with acute AN.

One measure that has been used extensively in individuals with ASD is the social responsiveness scale (SRS; Constantino & Gruber, 2005). The SRS is a 65 item parent- or teacher-rated questionnaire and is often administered as part of a comprehensive diagnostic assessment of ASD in those between the ages of 4 and 18 (Duku et al., 2013). More recently, an adult self-report version was developed (SRS-2; Constantino & Gruber, 2012). Like the original SRS, the SRS-2 comprises five subscales based on diagnostic criteria for ASD: social motivation; social awareness; social cognition; social communication; and restricted interests and repetitive behaviour. Total scores can be converted into *T*-scores in order to give an indication of severity of an individual's symptoms. *T*-scores falling within the mild, moderate, or severe range suggest clinically significant symptoms with varying degrees of impact on everyday social interactions. Dimensions of the SRS-2 have been found to correspond to the DSM-5 criteria domains for ASD (Frazier et al., 2014), and total scores discriminate those with ASD from non-ASD clinical populations (Takei et al., 2014). The SRS-2 also shows good concurrent and convergent and concurrent validity, correlating with measures of adaptive behaviour and the ADI-R in adults with ASD (Chan, Smith, Hong, Greenberg, & Mailick, 2017). Further, experimental evidence suggests that higher scores on the SRS-2 are associated with reduced social attention in those with ASD, one of the core characteristics of the disorder (Dijkhuis, Gurbuz, Ziermans, Staal, & Swaab, 2019; Hanley et al., 2015; Ketelaars et al., 2017) To date, no study has used the SRS-2 in individuals with AN.

The primary aim of the current study was to examine associations between scores on the SRS-2 and scores on an observational diagnostic measure, the ADOS-2, in adults with AN. Because the SRS-2 has not yet been used in this clinical population, we also aimed to explore group differences in SRS-2 scores between individuals currently ill with AN compared to recovered AN and HCs. Finally, the study aimed to examine associations between SRS-2 scores, ED severity, and functional impairment.

2 | METHODS

2.1 | Participants and design

The study was cross-sectional with three groups: acute AN, recovered AN (REC), and HCs. Ethical approval was obtained from the National Health Service (NHS) Research Ethics Committee (Camberwell St Giles, 17/LO/1960). All participants were required to be between 18 and 55 years old and fluent in English. A history of brain trauma or learning disability was exclusion criteria. HC participants were recruited through a King's College London email circular and posters around campuses. HCs were screened using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV; First, Williams, Karg, & Spitzer, 2015), to ensure they did not meet criteria for any psychiatric disorders. They were also required to have a body mass index (BMI) between 19 and 27.

In addition to the university advertisements, participants with AN or REC were recruited through online advertisements (B-eat, call for participants, MQ mental health). Participants with AN were also recruited through two specialist NHS ED services in London. AN and REC were screened using the SCID-5-RV to confirm a current or past diagnosis of AN. Participants with AN were required to have a BMI $\leq$18.5 and REC participants a BMI between 19 and 27. Further, REC participants were required to have maintained a BMI within this range for at least 1 year prior to testing.

2.2 | Procedure and materials

Participants attended a testing session as part of a wider study on socio-emotional processing at the Institute of

Psychiatry, Psychology & Neuroscience; however, where participants were inpatients ($N = 11$), testing took place at their place of treatment. Written informed consent was obtained, and the following measures were administered in order:

The Wechsler Abbreviated Scale of Intelligence – second edition (WASI-II; Wechsler, 2011) was used to estimate IQ. The two subtest version was used (vocabulary and matrix reasoning).

The Autism Diagnostic Observation Schedule – second edition (ADOS-2; Lord et al., 2012) is a standardised semi-structured observational interview for the assessment of ASD. Module 4 is intended for use with verbally fluent adults and thus was used in this study. The interview includes a range of questions and activities designed to evoke behaviours and cognitions associated with ASD. Items are scored on a scale of 0–3, with higher scores indicating more autistic behaviour. The revised algorithm, which was designed to more closely reflect the DSM-5 criteria for ASD was used for scoring (Hus & Lord, 2014). The algorithm has two subscales: social affect and restrictive and repetitive behaviours, and total scores of 8 or more indicate possible ASD. The interview was administered by the first author, who met requirements for ADOS-2 research reliability.

The SRS-second edition, adult self-report form (SRS-2; Constantino & Gruber, 2012) is a 65-item questionnaire assessing symptoms associated with ASD, with higher scores indicating more autistic symptoms. There are five sub-scales: social awareness (ability to recognise social cues, for example, item 7, "I am usually aware of how others are feeling"), social cognition (interpreting social behaviour, for example, item 48, "I have a good sense of humor and can understand jokes"), social communication (reciprocal communication in social situations, for example, item 16, "I avoid eye contact or am told that I have unusual eye contact"), social motivation (motivation to participate in social interactions, for example, item 6, "I would rather be alone than with others"), and restrictive interests and repetitive behaviour (circumscribed interests and stereotypy, for example, item 24, "I have more difficulty than others with changes in my routine"). Respondents indicate their agreement with each item on a four-point Likert scale, rating their behaviour over the past 6 months. The sum of all items is calculated to provide a total score (max 195). *T*-scores are interpreted as: $\leq 59T$, within normal limits; 60–65 *T*, mild; 66–75 *T*, moderate; $\geq 76T$ severe range. Cronbach's alpha was 0.97.

The Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994) was used to measure severity of ED psychopathology. Global scores are calculated by averaging responses across items, with higher scores indicating more severe symptoms (max 6). HCs with a score of >2.7 were excluded to ensure those with possible sub-threshold ED symptoms were not included (Lang et al., 2016). Cronbach's alpha was 0.98.

The Work and Social Adjustment Scale (WSAS; Mundt, Marks, Shear, & Greist, 2002) is a brief measure of functional impairment in five domains: work, home management, social leisure, private leisure, and ability to form and maintain close relationships. Scores range from 0 to 40, with a score of 20 or more indicating clinical significance. Cronbach's alpha was 0.93.

Participants' heights and weights were taken to calculate BMI (weight/height^2).

2.3 | Analytic plan

Histograms and Q-Q plots were inspected to check for normal distributions. Where data were positively skewed, a logarithmic transformation was applied. Homogeneity of variances was assessed using Levene's test. Group differences on continuous variables were examined using one-way ANOVAs and Tukey's post-hoc tests, or Welch's ANOVA with Games-Howell post-hoc tests where the assumption of homogeneity was violated. Group differences on dichotomous variables were assessed using chi-squared tests of homogeneity (or Fisher's exact test where the sample size assumption was not met). Zero-order correlations were calculated to examine associations between SRS-2 and ADOS-2 scores, ED severity (BMI, EDE-Q scores, illness length), and functional impairment (WSAS scores). Where significant correlations were found, regression analyses were run to examine whether SRS-2 scores predicted ADOS-2 scores, ED severity, and functional impairment.

3 | RESULTS

3.1 | Demographic information

One hundred and fifty-three participants were recruited. Out of 51 HCs, 5 were excluded based on their EDE-Q scores, and 1 REC participant was excluded as their BMI was above 27. A further 2 HCs, 1 REC, and 2 AN did not complete the SRS-2 and were thus excluded from analyses. Thus, data from 44 HCs, 49 REC, and 49 AN are presented here. Demographic information is presented in Table 1. Groups were of similar age, sex, and IQ. Over half of individuals with AN (53.5%) reported having at least one comorbid psychiatric disorder, compared to 38.8% of those in the REC group. The most common were depressive disorders (32.6% of AN, 18.4% of REC) and anxiety disorders (30.2% of AN, 22.4% of REC).

3.2 | ASD symptoms

Group differences on the SRS-2 and ADOS-2 are displayed in Table 2. Generally, SRS-2 total and subscale scores were significantly higher in both AN and REC compared to HCs. The exception was social awareness, where scores in REC did not significantly differ from that of AN or HC, lying in the middle. AN scored significantly higher than HC on ADOS-2 total and subscale scores. In addition, a significantly higher proportion of individuals with AN (26.5%) and REC (24.5%) scored above the ADOS-2 clinical cut-off compared to HCs (4.5%) ($X^2 = 8.73$, $p = .01$).

The distribution of SRS-2 T-scores is displayed in Figure 1. Ninety-one percent of HCs scored within the "normal" range, compared to 32.7% of participants with AN, and 53.1% of REC. Of the HCs, 4.5% scored within the "mild" range, compared to 18.4% of participants with AN and 16.3% of REC. Similarly, 4.5% of HCs scored within the "moderate" range, compared to 24.5% of participants with AN and 18.4% of REC. Finally, 24.5% of participants with AN and 12.2% of REC scored within the "severe" range, while no HCs did.

3.3 | Associations between ASD measures

Associations between the SRS-2 and ADOS-2 in AN and REC groups are presented in Table 3. SRS-2 total scores

TABLE 1 Mean (SD) demographic information

	AN ($N = 49$)	REC ($N = 49$)	HC ($N = 44$)	Test statistics	p-value	$\eta p^2/d$
Age (years)[†]	27.14 (8.78)	26.0 (8.1)	23.54 (4.59)	F(2, 89.41) = 2.32	.10	.03
% female	93.2	98.0	93.9	Fisher's exact test = 1.46	.63	
BMI	15.72 (1.44)[a]	21.14 (1.91)[b]	21.70 (1.91)[b]	F(2, 140) = 167.81	**<.001**	.71
Years of education	16.14 (3.18)	16.52 (2.62)	16.62 (2.49)	F(2, 132) = 0.36	.70	.01
IQ	110.21 (12.91)	110.16 (10.81)	114.21 (6.82)	F(2, 138) = 2.15	.12	.03
Illness length (years)	7.77 (7.86)	5.40 (5.65)	—	t(87.21) = 1.69	.09	.35
% on psychiatric medication	55.1[a]	32.7[b]	—	$X^2 = 5.39$	**.02**	

Note: Different superscripts indicate significant differences between groups, significant p-values are highlighted in bold.
[†]Variable was log transformed for analyses, original values are displayed.
Abbrevitaions: AN, anorexia nervosa; BMI, body mass index; HC, healthy control; IQ, intelligence quotient; REC, recovered anorexia nervosa; SD, standard deviation.

TABLE 2 Mean (SD) total and subscale scores on the SRS-2 and ADOS-2

	AN (N = 49)	REC (N = 49)	HC (N = 44)	Test statistics	p-value	ηp^2
SRS-2 total	85.29 (32.78)[a]	70.04 (31.97)[a]	39.23 (20.18)[b]	F(2,90.14) = 39.08	**<.001**	.30
Social awareness	8.73 (2.81)[a]	7.59 (3.27)	6.48 (2.45)[b]	F(2,139) = 7.14	**<.001**	.09
Social cognition	13.92 (6.86)[a]	11.08 (6.32)[a]	5.93 (4.83)[b]	F(2,92.03) = 23.51	**<.001**	.23
Social communication	27.24 (11.47)[a]	22.08 (11.88)[a]	12.75 (8.42)[b]	F(2,91.94) = 26.21	**<.001**	.24
Social motivation	19.08 (7.01)[a]	15.98 (6.96)[a]	8.52 (4.03)[b]	F(2,88.78) = 48.78	**<.001**	.33
Restricted interests and repetitive behavior	16.31 (8.40)[a]	13.31 (7.83)[a]	5.55 (3.99)[b]	F(2,85.47) = 41.95	**<.001**	.29
ADOS-2 total	5.37 (4.49)[a]	4.16 (4.50)	2.70 (2.56)[b]	F(2,88.52) = 6.81	**.002**	.07
ADOS-2 social affect	4.67 (4.11)[a]	3.71 (3.96)	2.52 (2.40)[b]	F(2, 89.32) = 5.26	**.007**	.06
ADOS-2 restricted and repetitive behaviors	0.69 (1.02)[a]	0.45 (0.89)	0.18 (0.58)[b]	F(2, 89.71) = 4.86	**.010**	.06

Note: Different superscripts indicate significant differences between groups, significant p-values are highlighted in bold.
Abbreviations: ADOS-2, autism diagnostic observation schedule, second edition; AN, anorexia nervosa; HC, healthy control; REC, recovered anorexia nervosa; SD, standard deviation; SRS-2, social responsiveness scale, second edition.

were significantly positively associated with ADOS-2 total scores and the SA subscale in both groups, but not the RRB subscale.

To ascertain whether SRS-2 scores predicted ADOS-2 classification (based on the clinical cut-off of 8) in the whole sample, a binomial logistic regression was run. The model was statistically significant, $X^2(1) = 20.97$, $p < .001$. The model explained 22% (Nagelkerke R^2) of the variance in ADOS-2 scores and correctly classified 84.5% of cases. The positive predictive value (PPV) was 77.78%, and the negative predictive value (NPV) was 84.96%.

3.4 | Associations between SRS-2 scores, ED severity, and functional impairment

In both AN and REC, SRS-2 total scores were significantly positively correlated with EDE-Q scores and degree of functional impairment (WSAS score), but not BMI or illness duration (see Table 4).

Multiple regression analyses were run to examine whether SRS-2 scores predicted EDE-Q and WSAS scores (Table 5). Group (acute or recovered AN) and BMI were also entered as covariates. Both models were significant (both $p < .001$). Along with group membership, SRS-2 total scores significantly added to the prediction of EDE-Q and WSAS scores.

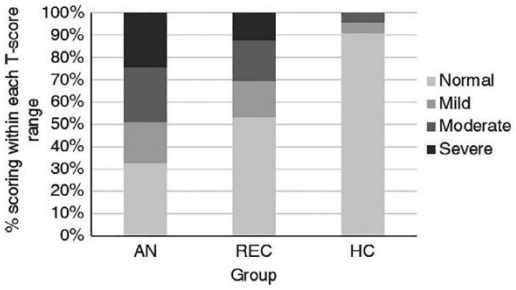

FIGURE 1 Proportion of participants scoring within each T-score range on the social responsiveness scale, adult self-report version (SRS-2)

4 | DISCUSSION

The main purpose of the current study was to examine whether scores on a widely used self-report measure of ASD symptoms, the SRS-2, were related to scores on a "gold-standard" diagnostic tool, the ADOS-2, in individuals with current or past AN. Indeed, there were significant positive correlations between measures, and SRS-2 scores significantly predicted ADOS-2 classification. Analyses of group differences revealed that individuals with AN and REC demonstrated significantly higher SRS-2 total and social cognition, social communication, social motivation, and restrictive interests and repetitive behaviour subscale scores. On the social awareness subscale, individuals with AN scored significantly higher than HCs, while REC showed an intermediate profile and did not significantly differ from either of the other two groups. Finally, ASD traits significantly predicted both severity of ED psychopathology and degree of functional impairment, but not BMI or illness duration.

The significant positive correlations between the SRS-2 and the ADOS-2 suggest the SRS-2 may be a useful tool for assessing ASD traits in individuals with AN both in research and clinical settings. Given the presence of

TABLE 3 Correlations between ASD measures

Group	Variables	1	2	3	4
AN	1. SRS-2 total	—			
	2. ADOS-2 total	.41**	—		
	3. ADOS-2 SA	.39**	.97***	—	
	4. ADOS-2 RRB	.22	.48***	.27	—
REC	1. SRS-2 total	—			
	2. ADOS-2 total	.47***	—		
	3. ADOS-2 SA	.51***	.99***	—	
	4. ADOS-2 RRB	.10	.66***	.53***	—

Note: ** = $p < .01$; *** = $p < .001$.

Abbreviations: ADOS-2, autism diagnostic observation schedule, second edition; AN, anorexia nervosa; ASD, autism spectrum disorder; REC, recovered anorexia nervosa; RRB, restricted and repetitive behaviours; SA, social affect; SRS-2, social responsiveness scale, second edition.

TABLE 4 Correlations between SRS-2 scores, ED severity, and WSAS scores

Group	Variables	1	2	3	4	5
AN	1. SRS-2 total	—				
	2. EDE-Q total	.31*	-			
	3. BMI	−.12	.06	—		
	4. Illness duration	−.01	−.03	−.14	—	
	5. WSAS	.69***	.42**	−.16	.20	—
REC	1. SRS-2 total	—				
	2. EDE-Q total	.46***	—			
	3. BMI	−.09	.11	—		
	4. Illness duration	−.10	−.01	−.21	—	
	5. WSAS	.57***	.59***	−.05	−.09	—

AN, anorexia nervosa; BMI, body mass index; ED, eating disorder; EDE-Q, eating disorder examination questionnaire; REC, recovered anorexia nervosa; SRS-2, social responsiveness scale, second edition; WSAS, work and social adjustment scale.
* = $p < .05$; ** = $p < .01$; *** = $p < .001$.

TABLE 5 Multiple regression analysis predicting EDE-Q and WSAS scores from SRS-2 scores

	EDE-Q			WSAS		
	b	SE_b	*β*	b	SE_b	*β*
SRS-2 total covariates	.02	.00	.32***	.17	.02	.53***
BMI	.10	.08	.18	−.16	.42	−.05
Group	−2.44	.50	−.70***	−8.42	2.65	−.40**
Adjusted R^2	.47			.58		

Abbreviations: BMI, body mass index; EDE-Q, eating disorder examination questionnaire; SE_b, standard error of the coefficient; SRS-2, social responsiveness scale, second edition; WSAS, work and social adjustment scale.
Note: ** = $p < .01$; *** = $p < .001$; *b*, unstandardized regression coefficient; *β*, standardized coefficient.

elevated ASD traits in AN is associated with poorer outcomes (Anckarsäter et al., 2012; Nielsen et al., 2015; Wentz, Gillberg, Anckarsäter, Gillberg, & Råstam, 2009), and less improvement during treatment (Stewart, McEwen, Konstantellou, Eisler, & Simic, 2017; Tchanturia, Larsson, & Adamson, 2016), accurate measurement and identification of possible cases is important. Correlations between measures were of medium strength in both AN and REC, and our findings were strengthened by a regression analysis, which showed that SRS-2 scores significantly predicted ADOS-2 classification (based on the clinical cut-off of 8). Studies using the SRS-2 and the ADOS-2 in individuals with ASD have demonstrated similar associations (Takei et al., 2014). It must be noted that scoring above the clinical cut-off on the ADOS-2 does not provide enough information to receive a diagnosis of ASD. In addition to the assessment of current ASD symptoms, a battery of measures are recommended, in order to obtain information about early developmental history, behavioural problems, functioning at home and in education or employment, comorbidities, and sensory sensitivities (NICE, 2012). Future research would benefit from using the SRS-2 in individuals with AN who have undergone a full ASD assessment.

Total SRS-2 scores were significantly higher in individuals with AN and REC compared to HCs, with a large effect size. Indeed, mean scores were similar to those that have been reported in adults with ASD (e.g., Dijkhuis et al., 2019; Maddox & White, 2015; Takei et al., 2014; Walsh, Baxter, Smith, & Braden, 2019). Further, around half of participants with AN scored within the "moderate" or "severe" impairment range, compared to just under one-third of REC, and only 4.5% of HCs. These findings are in agreement with previous studies demonstrating clinically significant levels of ASD traits in individuals with AN (Westwood & Tchanturia, 2017). Far less work has examined ASD traits in those who have recovered from AN, but generally studies show that elevated ASD traits persist after recovery (Bentz et al., 2017; Sedgewick et al., 2019). These results suggest that high ASD traits seen in those with AN are not a result of starvation or other state effects, although longitudinal research is required. Participants with AN and REC also demonstrated significant impairments across the SRS-2

subscales, with large effect sizes. The exception was social awareness, where scores in the REC group did not differ from the other two groups, and the magnitude of the effect size for the group difference between AN and HC was also smaller. Females with ASD are reported to show greater awareness of the need for social interaction than males with the disorder (Lai, Lombardo, Auyeung, Chakrabarti, & Baron-Cohen, 2015); therefore, a possible explanation for our findings may relate to the predominantly female sample included in the study.

In accordance with our findings in recovered AN, the lack of an association between BMI and SRS-2 scores suggests that elevated ASD symptoms do not merely reflect increased rigidity and social withdrawal that can accompany starvation. Our findings do however suggest an association between increased severity of ED psychopathology and ASD traits in both acute and recovered AN. This finding is in agreement with a previous study demonstrating a positive association between AQ-10 scores and scores on the EDE-Q in a large sample of inpatients with AN (Tchanturia, Adamson, Leppanen, & Westwood, 2019). Our study went further by showing that SRS-2 scores explained a significant proportion of the variance in EDE-Q scores, however the exact nature of this relationship is not known. Why might ASD symptoms exacerbate ED symptoms? The cognitive interpersonal maintenance model of AN proposes that cognitive rigidity, increased attention to detail, and sensitivity to order are predisposing traits for the illness (Treasure & Schmidt, 2013). Once dieting behaviour is triggered, it is undertaken in a highly meticulous and rigid manner, and the ensuing lack of nutrition further serves to reduce central coherence and increase the narrow focus on food and weight. Thus, it may be that these neuropsychological traits characteristic of ASD perpetuate ED cognitions and behaviours. Another possibility is that the social difficulties associated with ASD lead to isolation, allowing ED cognitions and behaviours to dominate. Indeed, social difficulties have been shown to be an important prognostic factor in AN, predicting poorer outcomes (Franko et al., 2013; Wentz et al., 2009; Zipfel, Löwe, Reas, Deter, & Herzog, 2000). Qualitative work has also emphasised the importance of social support and decreasing isolation as key to recovery (Cockell, Zaitsoff, & Geller, 2004; Federici & Kaplan, 2008; Linville, Brown, Sturm, & McDougal, 2012). Finally, it may be the case that some other factor not measured in this study influences both EDE-Q and SRS-2 scores; therefore, replication of our findings in other samples are required.

Similar to past findings in ASD (Chan et al., 2017; Mason et al., 2018), SRS-2 scores significantly predicted functional impairment, providing further evidence supporting the utility of the instrument in individuals with AN. As well as using the SRS-2 to identify individuals who may require further ASD assessment, the subscale scores could give valuable information on the specific areas of difficulty with which an individual presents. If appropriate, these could be incorporated into an individualised treatment approach. For example, social skills training might be useful for someone who shows difficulties in the social cognition domain. Group social skills interventions are effective in improving communication, social anxiety, and social functioning in adults with ASD (Spain & Blainey, 2015; Spain, Blainey, & Vaillancourt, 2017). Such interventions could be useful for those with AN, especially those with high ASD traits. On the other hand, cognitive remediation therapy (CRT) may benefit someone with high scores on the restricted interests and repetitive behaviour subscale of the SRS-2. Preliminary evidence suggests that CRT increases set-shifting performance in those with AN and ASD traits (Dandil, Smith, Adamson, & Tchanturia, 2019). Whether the SRS-2 is sensitive to treatment-related changes in individuals with AN is an interesting question for future research. When using the SRS-2, clinicians should advise patients that although it is not a diagnostic tool, the SRS-2 does correlate strongly with other diagnostic measures and could provide indications about some of the challenges they are facing that may not have previously been well thought about in treatment. This might enhance complex formulations and help to guide more efficient and effective treatments. It may also help the patient to think about what sort of additional support they might need as they leave hospital and continue their recovery from AN in the community. The results might also be shared with the person's family and carer support network, with the person's permission and involvement, so that loved ones might make a start on better understanding the person's strengths and challenges.

The study has several limitations. First, only a small proportion of males were included, and as a result, we were unable to examine whether SRS-2 scores differed by sex, or indeed whether SRS-2 and ADOS-2 scores were similarly correlated in males and females. To date, studies exploring ASD traits in individuals with AN have almost all included exclusively female samples, and it is not yet known whether the proportion of males with AN and high ASD traits is similar to that of females. There is evidence to suggest that females with ASD show lower scores compared to males with ASD on diagnostic interviews such as the ADOS-2, despite showing similar or higher scores on self-report measures of symptoms (Frazier, Georgiades, Bishop, & Hardan, 2014; Lai et al., 2011; Mason et al., 2018). The scoring algorithms used in diagnostic interviews may be biased towards identification of male-typical presentations, given the

longstanding male predominance in ASD case identification (Lai et al., 2015). Relatedly, females with ASD may use more compensatory strategies, showing better social communication than males, despite similar levels of underlying difficulties and distress (Lai et al., 2017). One might expect then that an even greater proportion of males with AN may score above the ADOS-2 cut-off than females with AN; however, this remains a question for future research.

Second, while the ADOS-2 is recommended for use in diagnostic assessments of ASD, alone it does not provide enough information to give a diagnosis. The current study would benefit from including a group of individuals with AN who hold a confirmed diagnosis of ASD, in order to better test the predictive power of the SRS-2 as a screening tool. Third, the cross-sectional design should be noted when interpreting group differences between the acute and REC groups. It is possible that differences in ED or ASD psychopathology contributed to the recovery of the REC group. Research examining ASD traits longitudinally in individuals with AN would provide stronger evidence to delineate state versus trait effects. Finally, a history of psychiatric disorders was an exclusion criteria for HCs; however, comorbidities were allowed in individuals in the AN and REC groups, introducing a potential confound to the results. Relatedly, we were unable to corroborate comorbid psychiatric diagnoses in AN and REC participants via psychiatric interviews, therefore, preventing an analysis of the potential confounding effect of anxiety and depression on ASD symptoms. Although there is evidence to suggest that ADOS-2 scores are largely unrelated to anxiety and depression in individuals with AN (Sedgewick et al., 2019), it is not yet known whether SRS-2 scores are influenced by affective symptoms in this population. Indeed, many of the items on the SRS-2 are also symptoms of disorders such as social anxiety (e.g., lack of eye contact, discomfort in social situations). Investigations into the trajectory of symptoms over time may be useful in clarifying this issue.

5 | CONCLUSION

Recent evidence has accumulated to suggest an association between AN and ASD, raising important questions for both research and clinical practice. Currently, there is a lack of agreement on which tools should be used to assess ASD in individuals with AN. To our knowledge, this is the first study to use the SRS-2 in a sample of adults in the acute and recovered stages of AN. In agreement with previous studies showing high ASD traits in those with AN, participants in the acute and recovered stage of AN scored significantly higher on the SRS-2 compared to age- and sex-matched HCs. Scores on the SRS-2 significantly predicted ADOS-2 classification in the whole sample, suggesting the SRS-2 may be useful in identifying individuals with suspected ASD whose symptoms may benefit from further investigation. Positive associations between SRS-2 scores, functional impairment, and ED psychopathology further support the utility of the measure within this population. Replications in larger samples are required to confirm the reliability of our results, and future research should employ longitudinal designs in order to examine illness versus trait factors that may influence ASD symptoms in AN.

ACKNOWLEDGEMENTS

Jess Kerr-Gaffney is supported by the Economic and Social Research Council (ESRC). The research was supported by the Psychiatry Research Trust and Swiss Anorexia Nervosa Foundation (ref: 58-16). Kate Tchanturia would like to acknowledge support from MRC Child and Young Adult Mental Health (ref: MR/R004595/1) and the Health Foundation (ref: 1115447). We would like to thank the participants who took part in the research for their time and the clinicians for their support in recruitment.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Kerr-Gaffney J, Harrison A, Tchanturia K. The social responsiveness scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa. *Eur Eat Disorders Rev*. 2020;1–12. https://doi.org/10.1002/erv.2736

Chapter 4 - Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach

Kerr-Gaffney, J. E., Halls, D., Harrison, A., & Tchanturia, K. (2020). Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach. *Frontiers in Psychiatry, 11,* Article 401. https://doi.org/10.3389/fpsyt.2020.00401

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 12 May 2020
doi: 10.3389/fpsyt.2020.00401

Exploring Relationships Between Autism Spectrum Disorder Symptoms and Eating Disorder Symptoms in Adults With Anorexia Nervosa: A Network Approach

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Specialty section:
This article was submitted to Psychosomatic Medicine, a section of the journal Frontiers in Psychiatry

Received: 30 March 2020
Accepted: 21 April 2020
Published: 12 May 2020

Citation:
Kerr-Gaffney J, Halls D, Harrison A and Tchanturia K (2020) Exploring Relationships Between Autism Spectrum Disorder Symptoms and Eating Disorder Symptoms in Adults With Anorexia Nervosa: A Network Approach. Front. Psychiatry 11:401. doi: 10.3389/fpsyt.2020.00401

Over the past few decades, research has accumulated to suggest a relationship between anorexia nervosa (AN) and autism spectrum disorder (ASD). Elevated ASD traits are present in around one third of those with AN, and there is some evidence to suggest that ASD traits are associated with more severe eating disorder (ED) psychopathology. The current study aimed to examine relationships between ED and ASD symptoms in individuals with a lifetime history of AN using network analysis. One hundred and one participants completed the ED Examination Questionnaire (EDE-Q) and the Social Responsiveness Scale (SRS-2). A regularized partial correlation network was estimated using a graphical least absolute shrinkage and selection operator. Expected influence (EI) and bridge EI values were calculated to identify central and bridge symptoms respectively. Isolation, difficulties with relating to others, and feelings of tension during social situations were most central to the network, while poor self-confidence, concerns over eating around others, and concerns over others seeing one's body were the strongest bridge symptoms. Our findings confirm that interpersonal problems are central to ED psychopathology. They also suggest poor self-confidence and social anxiety-type worries may mediate the relationship between ED and ASD symptoms in those with a lifetime diagnosis of AN. Longitudinal studies examining fluctuations in symptoms over time may be helpful in understanding direction of causality.

Keywords: anorexia nervosa, comorbidity, autism spectrum disorder, self-report, social behavior

INTRODUCTION

Over the past few decades, evidence suggesting a relationship between autism spectrum disorder (ASD) and anorexia nervosa (AN) has accumulated (1, 2). ASD is a neurodevelopmental disorder characterized by difficulties in social communication and interaction, as well as restrictive, repetitive patterns of behavior or interests (3). ASD is a lifelong condition, and is more commonly diagnosed

in males than females (4). On the other hand, AN is a severe eating disorder (ED) associated with persistent restriction of energy intake, fear of weight gain, and disturbances in the way in which one's body shape or weight is experienced (3). AN is more prevalent in females, and peak age of onset is in late adolescence (5, 6).

Despite the apparent differences between the two disorders, empirical research has shown a number of similarities in the phenotypic expressions of AN and ASD. For example, in the socio-emotional domain, considerable research has documented difficulties in emotion recognition (7), empathy (8), and theory of mind (ToM) (9) in individuals with ASD. These difficulties are also seen in those with AN, although are often less pronounced than is seen in ASD (10–12). Furthermore, high levels of alexithymia (13, 14), social anxiety (15, 16), and differences in social attention (17–19) are associated with both disorders. In the neurocognitive domain, both AN and ASD are associated with weak central coherence (20, 21), increased attention to detail (22, 23), and difficulties in set-shifting (24, 25), an executive function that allows for flexible thinking and behavior.

As well as these similarities in socio-emotional and neurocognitive profiles, those with AN show high levels of ASD traits. For example, it is reported that between 4% and 52.5% of individuals with AN score above clinical cut-offs on diagnostic assessment tools for ASD1. It has been suggested that high levels of ASD traits found in a proportion of those with AN may be due to the effects of starvation, and do not represent true ASD (26). However, several studies have found that body mass index (BMI), which is often used as a measure of illness severity, is not associated with ASD traits in individuals with AN (27–33). A few of these studies also examined associations with illness duration, finding that those with high ASD traits had not been ill for a significantly longer period of time than those with low ASD traits (29, 33). Finally, a significant proportion of individuals recovered from AN also show elevated ASD traits compared to HCs (27, 30, 34). Therefore, it seems the association between ASD and AN is not a product of starvation, yet the exact nature of the relationship remains unclear.

However, there is some evidence to suggest that ASD symptoms are positively associated with severity of ED psychopathology in those with AN. For example, in a large sample of inpatients with AN, Tchanturia et al. (31) reported that scores on the Autism Quotient (AQ) (35) were positively associated with scores on the ED Examination Questionnaire (EDE-Q) (36). A similar association between AQ scores and ED symptoms has been reported in nonclinical populations (37, 38). Further, the presence of ASD traits in AN is associated with more frequent and longer inpatient stays (29), less improvement during treatment (39, 40), and poorer outcomes (41–43). Why might a more severe ED presentation be associated with high ASD traits? One possibility is that some of the neurocognitive traits associated with ASD, such as cognitive rigidity, increased attention to detail, and sensitivity to order may perpetuate a narrow focus on food and weight in individuals with AN and make change difficult (44). Indeed, Westwood and colleagues (45) reported that individuals with AN and high ASD traits showed higher levels of cognitive rigidity and set-shifting difficulties than individuals with low ASD traits. As well as a significant proportion of individuals with AN showing high levels of ASD traits on dimensional measures, a number of studies have found that 8%–29% meet full diagnostic criteria for ASD (34, 41, 46–49). Given that social difficulties are an important predictor of poor outcomes in AN (43, 50–52), another possibility is that those with comorbid ASD and AN have particularly poor outcomes due to the social communication difficulties associated with ASD. Yet another possibility is that avoidance of certain foods due to sensory sensitivities in ASD may reinforce food restriction. Such hypotheses remain to be tested empirically.

A potentially useful method for examining the nature of the relationship between AN and ASD symptoms is provided by network theory. Network theories of psychopathology represent psychiatric disorders as constellations of symptoms, activating one another (53). The relationships between symptoms are key to the development and maintenance of psychopathology; symptoms can form feedback loops, eventually producing a set of symptoms that are recognized as a psychiatric disorder. This theory has important implications for understanding comorbidity. Symptoms are often shared among different psychiatric disorders, for example feelings of guilt are common in obsessive compulsive disorder (OCD) and are also a central feature of major depression (3). Because symptoms in a network have causal relationships with one another, clusters of symptoms belonging to one disorder can activate those of another disorder, resulting in diagnostic comorbidity (54).

Psychological networks can be estimated using network analysis. Networks are made up of nodes (symptoms) and edges (relationships between symptoms). It is possible to calculate which nodes or symptoms have most connections in the network (node centrality) and therefore are most important in maintaining psychopathology. Further, it is possible to calculate which symptoms of a given disorder are most connected to symptoms in another disorder cluster (bridge nodes), and therefore may maintain comorbidity. Currently, only a few studies have examined comorbidity using network analysis in individuals with EDs. These studies have most often focussed on comorbidity between anxiety and ED symptoms, finding that avoidance of social eating is an important bridge symptom (55–57). Others have examined depression (55, 58) and OCD symptoms (59), however no study to date has focussed on ASD and ED symptom comorbidity.

The aim of the current study was to examine relationships between ED and ASD symptoms in individuals with AN using network analysis. Because ASD symptoms have been shown to persist in individuals recovered from AN, suggesting independence from clinical state, our sample included those with a current or past diagnosis of AN. We aimed to identify central nodes in order to understand which symptoms may be most important in maintaining the symptom network as a whole. Bridge nodes were also identified in order to detect symptoms most important in explaining potential comorbidity of AN and ASD.

MATERIALS AND METHODS

Participants

The study was cross-sectional. Ethical approval was obtained from the National Health Service (NHS) Research Ethics Committee (Camberwell St Giles, 17/LO/1960). Participants provided their written informed consent to participate in the study. Participants with a lifetime history of AN were recruited from two specialist NHS ED services in London, online advertisements, and through the King's College London university research recruitment email. Participants were required to be between 18 and 55 years old and fluent in English. Exclusion criteria were a history of brain trauma or learning disability. A past or current diagnosis of AN was confirmed using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV) Module I "Feeding and Eating Disorders" (60).

Procedure and Materials

Participants attended a testing session as part of a wider study on socio-emotional processing at the Institute of Psychiatry, Psychology & Neuroscience, however where participants were inpatients, testing took place at their place of treatment. Written consent was obtained, and the following measures administered:

The EDE-Q (36) was used to measure severity of ED psychopathology. Twenty-two of the 28 items are rated for frequency during the past 28 days on a seven-point Likert scale, with higher scores indicating more eating, shape, or weight concerns and behaviors. The remaining six items assessing frequency of various behaviors are not included in total or subscale score calculations, as these items can take on any value. The EDE-Q demonstrates good psychometric properties, correlating with measures of similar constructs (61). Cronbach's alpha was 0.91.

The Social Responsiveness Scale-2nd edition, adult self-report form (SRS-2) (62) is a 65-item questionnaire assessing symptoms associated with ASD, with higher scores indicating more autistic symptoms. There are five subscales: social awareness (ability to recognize social cues), social cognition (interpreting social behavior), social communication (reciprocal communication in social situations), social motivation (motivation to participate in social interactions), and restrictive interests and repetitive behavior (circumscribed interests and stereotypy). Respondents indicate their agreement with each item on a four-point Likert scale, rating their behavior over the past six months. The SRS-2 has been used extensively in ASD research, and is also recommended for use in diagnostic assessments in adults with ASD (63). Validation studies have found measurement invariance across the sexes, and few sex, age, or rater effects (64–66). Scores on the SRS-2 have been shown to predict whether individuals with AN score above the clinical cut-off on the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) (67), a "gold-standard" clinical interview measure for ASD (68). Cronbach's alpha was 0.96.

Demographic information was also collected, along with weight and height measurements to calculate BMI (height/weight^2).

Network Analysis

Analyses were performed in R version 3.6.1 (69). R codes are provided in the **Supplementary Information**.

Item Selection

Network analysis assumes that each node in the network represents a distinct construct. Given that some of the questionnaire items are very similar in content, the goldbricker function in R package *networktools* (70) was used to select items to include in the network. Goldbricker compares dependent overlapping correlations (i.e., items with high multicollinearity) for all items in the network. If a certain proportion of correlations between node A and all other nodes do not significantly differ from those between node B and all other nodes (e.g., items share ≥75% of correlations), nodes A and B are assumed to be overlapping items measuring the same construct ("bad pairs"). One of the nodes is subsequently removed. The 22 Likert items from the EDE-Q and all 65 items from the SRS-2 were entered. After dropping the bad pairs, 18 EDE-Q and 55 SRS-2 items were left for inclusion in the network. The full list of EDE-Q and SRS-2 items and those included in the network are provided in the **Supplementary Information**.

Network Estimation and Accuracy

A regularized partial correlation network with weighted edges was estimated using a graphical least absolute shrinkage and selection operator (LASSO) using the *qgraph* R package (71). This method limits the total sum of absolute parameter values and drops edges that are close to zero out of the model, keeping only those that are most robust and likely to represent genuine associations. The tuning parameter (λ) was set to 0.25. This value is typically set between 0 and 0.5, with higher values resulting in simpler models with fewer edges, and lower values favoring discovery but more likely to estimate spurious edges (72).

Accuracy of edge-weights were assessed using nonparametric bootstrapping using the *bootnet* package (73). Bootstrapping involves repeatedly estimating a model under sampled or simulated data and estimating the statistic of interest, in this case, edges. The bootstrapped 95% confidence intervals (CIs) indicate the sampling variation, and the strength of a given edge is difficult to interpret if bootstrapped CIs are wide. Correlation stability (CS) coefficients were calculated to assess the stability of expected influence (EI) and bridge EI. In this case, a case-dropping bootstrap is used to indicate whether the centrality indices remain the same after reestimating the network using only a subset of cases from the sample. The CS coefficient indicates the proportion of the sample that can be dropped to retain a correlation >0.7 with the original sample. It should not be below 0.25, and preferably above 0.5 (73). Finally, bootstrapped difference tests (a = 0.05) were run to test for significant differences in centrality indices between nodes.

Network Interpretation

Central nodes were identified by calculating EI using the *networktools* package. EI is similar to the more commonly used metric, strength, as it is calculated by summing all of the edges a

given node has with all other nodes in a network. However unlike strength, which does not distinguish between positive and negative edges, EI accounts for the direction of associations. This is an important distinction in networks which include psychopathological symptoms of more than one disorder, where some negative relationships are likely (74).

Bridge nodes were identified by calculating bridge EI using the *networktools* package. Both bridge EI one-step (bridge EI1) and bridge EI two-step (bridge EI2) were calculated. Bridge EI1 identifies the strength and directionality of the relationships a node in one cluster has with all nodes of another cluster. Bridge EI2 additionally takes into account the secondary influence of a node *via* the influences of its immediate neighbors. For centrality and bridge indices, higher values represent greater influence. Z-scores are reported throughout for ease of interpretation.

RESULTS

Sample Characteristics

In total, 101 participants took part in the study. Fifty-one were acutely ill with AN, while fifty were recovered. Demographic and clinical information is displayed in **Table 1**. On the SRS-2, 43% of participants scored within the "normal" range, scores within this range are not associated with clinically significant symptoms. Seventeen percent of participants scored within the "mild" range, indicating deficiencies in reciprocal social behavior that are clinically significant and may lead to mild to moderate interference with daily living. A further 21% scored within the "moderate" range, indicating clinically significant difficulties which lead to substantial interference with social behavior. Finally, 19% of participants scored in the "severe" range, indicating severe and enduring difficulties with social behavior. Scores within the moderate and severe range are typical for individuals with a diagnosis of ASD.

Network Estimation and Accuracy

Questionnaire data from three participants contained missing values (representing 0.08% of the total questionnaire data). Given that nodes in our network did not rely on subscale or total score calculations from questionnaires, the rest of the data from these participants was included in analyses. The network structure composed of EDE-Q and SRS-2 symptom scores is displayed in **Figure 1**. Green edges represent positive relationships, while red indicates negative ones. The thicker the edge, the stronger the regularized partial correlation.

Plots displaying the bootstrapped CIs of estimated edge-weights, bootstrapped centrality indices, and bootstrapped differences tests are reported in the **Supplementary Material**. The EI CS coefficient was 0.67, and the bridge EI CS coefficient was 0.59, indicating both EI and bridge EI can be interpreted meaningfully (73).

TABLE 1 | Demographic and clinical information of participants with lifetime anorexia nervosa (AN) (N = 101).

	Mean (SD)	Range
Age (years)	26.95 (8.27)	18.16 – 54.59
% female	95.0	–
BMI	18.39 (3.25)	12.90 – 27.00
Years of education	16.33 (2.89)	10.00 – 27.00
Illness length (years)	6.47 (6.89)	0.50 – 35.00
% on psychiatric medication	43.6	–
EDE-Q total	2.84 (1.75)	0.00 – 5.69
SRS-2 total	77.66 (33.11)	17.00 – 160.00

AN, anorexia nervosa; BMI, body mass index; EDE-Q, eating disorder examination questionnaire; SRS-2, social responsiveness scale; SD, standard deviation.

Centrality

EI is plotted in **Figure 2**. The items with the highest EI were SRS-2 37 "I have difficulty relating to adults outside of my family," SRS-2 57 "I tend to isolate myself," and SRS-64 "I am much more tense in social situations than when I am by myself."

Bridge Nodes

Bridge EI values are plotted in **Figure 3**. For bridge EI1, the strongest ED bridge symptom was EDE-Q 21 "How concerned have you been about other people seeing you eat?", and the strongest ASD bridge symptom was SRS-11 "I have good self-confidence" (reverse coded). For bridge EI2, the strongest ED bridge symptom was EDE-Q 28 "How uncomfortable have you felt about others seeing your shape or figure", and the strongest ASD bridge symptom was again SRS-11 "I have good self-confidence."

DISCUSSION

The current study is the first to examine relationships between ED and ASD symptoms in individuals with past or current AN using network analysis. Constructing a network of partial correlations allowed us to examine connections between symptoms, independent of the effects of other symptoms in the network. Firstly, we aimed to identify core symptoms in the network. The three nodes with the highest centrality in the network were all SRS-2 items: SRS-2 37 "I have difficulty relating to adults outside of my family," SRS-2 57 "I tend to isolate myself", and SRS-64 "I am much more tense in social situations than when I am by myself." The former two items are from the social communication subscale of the SRS-2, while the latter is from the social motivation subscale. These results suggest that difficulties in social communication and isolation may be core symptoms in AN psychopathology, over and above conventional ED symptoms, such as weight and shape concern. However, it must be noted that the inclusion of recovered individuals, some of whom had rather low EDE-Q symptom scores may have influenced these results. Had our sample only included individuals in the acute stage of AN, EDE-Q items might have been more central to the network. Nonetheless, our study is not the first to demonstrate the importance of social difficulties in AN psychopathology. For example, Monteleone and colleagues (58) found that depression and personal alienation were the nodes with highest centrality in their network of symptoms in children and adolescents with AN. Personal alienation, a subscale of the EDs Inventory (EDI), reflects a sense of emotional emptiness, aloneness,

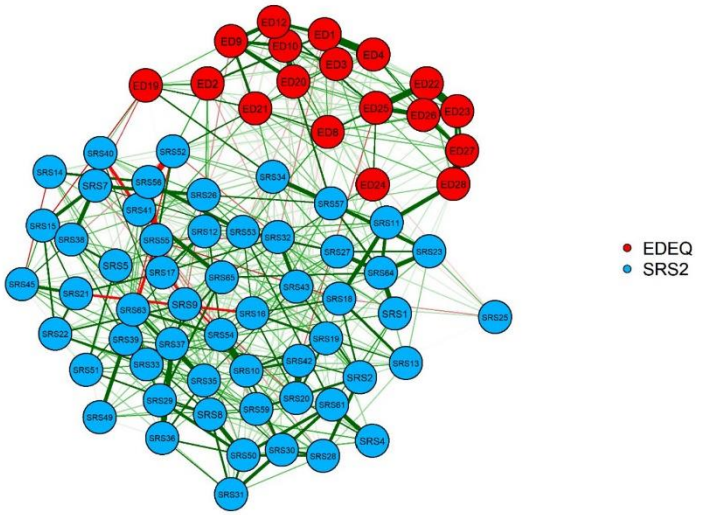

FIGURE 1 | Graphical least absolute shrinkage and selection operator network. Eating Disorder Examination Questionnaire (EDE-Q) items: ED1, limit food; ED2, fasting; ED3, excluding foods; ED4, eating rules; ED8, concentration affected by shape/weight; ED9, fear of loss of control; ED10, fear of weight gain; ED12, desire to lose weight; ED19, eating in secret; ED20, guilt over eating; ED21, concern over other people seeing you eat; ED22, weight overvaluation; ED23, shape overvaluation; ED24, reaction to weighing; ED25, weight dissatisfaction; ED26, shape dissatisfaction; ED27, uncomfortable seeing own body; ED28, uncomfortable over others seeing own body. Social responsiveness scale (SRS-2) items: SRS1, uncomfortable in social situations; SRS2, facial expressions; SRS4, rigid behavior; SRS6, prefer to be alone; SRS7, aware of others feelings; SRS8, strange behavior; SRS9, dependent on others; SRS10, take things literally; SRS11, good self-confidence; SRS12, communicate feelings; SRS13, awkward in turn taking interactions; SRS14, not well coordinated; SRS15, understand change in tone/facial expression; SRS16, avoid/unusual eye contact; SRS17, recognize unfairness; SRS18, difficulty making friends; SRS19, frustrated in conversations; SRS20, sensory interests; SRS21, imitate others'; SRS22, interact appropriately; SR23, avoid social events; SRS25, don't mind being out of step with others; SR26, offer comfort to others; SRS27, avoid starting social interactions; SRS28, think about the same thing over and over; SRS29, regarded as odd; SRS30, upset in situations with lots going on; SRS31, can't get mind off something; SRS32, good personal hygiene; SRS33, socially awkward; SRS34, avoid people who want to be emotionally close to me; SRS35, have trouble keeping up with conversations; SRS36, difficulty relating to family; SRS37, difficulty relating to adults outside family; SRS38, respond to others' moods; SRS39, interested in too few topics; SRS40, imaginative; SRS41, wander aimlessly between activities; SRS42, sensory sensitivity; SRS43, enjoy small talk; SRS45, interested in what others' are attending to; SRS49, do well at intellectual tasks; SRS50, repetitive behaviors; SRS51, difficulty answering questions directly; SRS52, overly loud; SRS53, monotone voice; SRS54, thing about people and objects in the same way; SRS55, invade others' personal space; SRS56, walk between two people; SRS57, isolate myself; SRS59, suspicious; SRS61, inflexible; SRS63, unusual greeting; SRS64, tense in social settings; SRS65, stare into space.

and feeling separated from others. Somewhat similar findings were reported by Somli and colleagues (75), who found that in adolescents and adults with AN, depression, anxiety, interpersonal sensitivity, and ineffectiveness were most central to the network. Interpersonal sensitivity, a subscale of the Symptom Checklist 90 (SCL-90), assesses feelings of inadequacy and inferiority in comparison to others, as well as self-consciousness and discomfort during social interactions.

Our second aim was to identify bridge nodes; those that connect ED and ASD symptom clusters. The strongest ASD bridge symptom was SRS-2 11 "I have good self-confidence" (reverse coded), while the strongest ED bridge symptoms were EDE-Q 21 "How concerned have you been about other people seeing you eat?" (bridge EI1) and EDE-Q 28 "How uncomfortable have you felt about others seeing your shape or figure?" (bridge EI2). The self-confidence item belongs to the social motivation subscale of the SRS-2. Our results suggest that a lack of self-confidence may be important in understanding the link between ED psychopathology and ASD symptoms in those with lifetime AN. However, it must be noted that low self-confidence is a rather nonspecific psychiatric symptom, commonly reported in depression, anxiety, substance abuse disorders, and EDs (76). Interestingly, our finding is very similar to that of Forrest and colleagues (56), who found that the low self-confidence item of the State-Trait Anxiety Inventory (STAI) was the strongest trait anxiety bridge node linked to ED symptoms in a mixed ED sample. It could be that elevated scores on ASD assessments found in individuals with AN are partly due to high anxiety, a symptom shared by both disorders. In an analysis of 18 previously published comorbidity networks, Jones and colleagues (54) observed that several symptoms emerged as bridge symptoms across multiple networks. The networks included several different disorders, including anxiety, bulimia nervosa (BN), OCD, depression, and ASD, and also used a wide variety of symptom scales. This demonstrates that certain symptoms may not only explain comorbidity between two

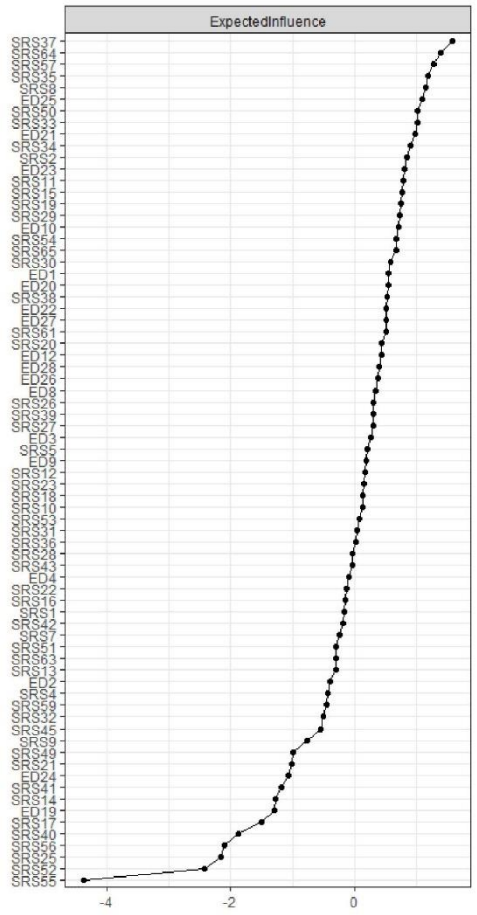

FIGURE 2 | Centrality plot depicting expected influence (EI) of each node. Values are given as Z scores, higher values represent greater centrality in the network.

disorders, but may be important transdiagnostic factors across psychiatric disorders.

Regarding ED bridge nodes, it is notable that both involve concern over being observed by others. The concern over others seeing you eat item has repeatedly been shown to be the strongest ED bridge node connecting ED and anxiety symptoms in those with AN (55) and mixed ED groups (56, 57). High social anxiety is a feature of both ASD (16, 77) and AN (15), and our findings might suggest that social anxiety worries are important in explaining comorbidity between AN and ASD. It has been hypothesized that some of the core symptoms of ASD may increase the risk of developing social anxiety (78, 79). For example, poor social skills or difficulties in recognizing emotions and mental states in others may lead to rejection from peers and isolation during formative years, factors which are implicated in the development of social anxiety disorder (SAD). There is also evidence to suggest that SAD may be a risk factor for the development of AN. In those with both disorders, SAD precedes AN onset in around two thirds of cases (80, 81). Fears around eating in front of others may lead to avoidance of social eating in those with SAD, a potential pathway by which other eating disordered behaviors may form. Qualitative work has also provided some insight into how these factors may interact and contribute to the development of AN. For example, Kinnaird et al. (82) found that participants with AN and ASD felt that their ED had developed as a way of dealing with the social confusion and difficulties relating to other people associated with their ASD. Participants also described how social difficulties, such as dealing with noise and social chat during meal times, made inpatient treatment difficult. Similarly, based on their qualitative study of AN and ASD comorbidity, Brede and colleagues (83) hypothesized that AN may develop through both direct and indirect pathways. In the indirect pathway, ASD-related difficulties are proposed to give rise to negative emotional consequences, and restrictive eating behaviors are employed as an attempt to cope with this. For example, individuals with ASD may have a longstanding history of being bullied and socially ostracized, resulting in low self-esteem and emotional distress. Restricting food intake can provide a sense of control and numbing of strong emotions. Given our study was cross-sectional, hypotheses about the direction of causality between symptoms are preliminary. Future longitudinal research using network analysis could help disentangle interactions between ASD, ED, and social anxiety symptoms.

Our findings have important theoretical and clinical implications. That the symptoms most central to the network all concerned social difficulties provides support for models emphasizing the role of interpersonal problems in the development and maintenance of AN. For example, the cognitive-interpersonal maintenance model of AN proposes that anxious, avoidant, and socio-emotional traits, including sensitivity to stress and negative emotions, anxious and avoidant attachment, and negative self-evaluations are predisposing factors (44). While some interpersonal difficulties are worsened by the ill state, this group of traits are proposed to be present before and after the illness, and often also in family members. Further, our results support the need for therapies to target interpersonal functioning as a key maintaining factor in individuals with AN, such as interpersonal psychotherapy (84), cognitive behavioral therapy (CBT) (85), and the Maudsley model of AN treatment for adults (MANTRA) (86). Secondly, it is of note that none of the items from the restrictive interests and repetitive behavior subscale of the SRS-2 had particularly high EI or bridge EI values. This may suggest that unlike social and communication difficulties, this group of symptoms play a relatively small part in AN and ASD comorbidity. Indeed, previous studies have shown that while social and communication difficulties are often elevated in those with AN, restricted and repetitive behaviors are often less pronounced

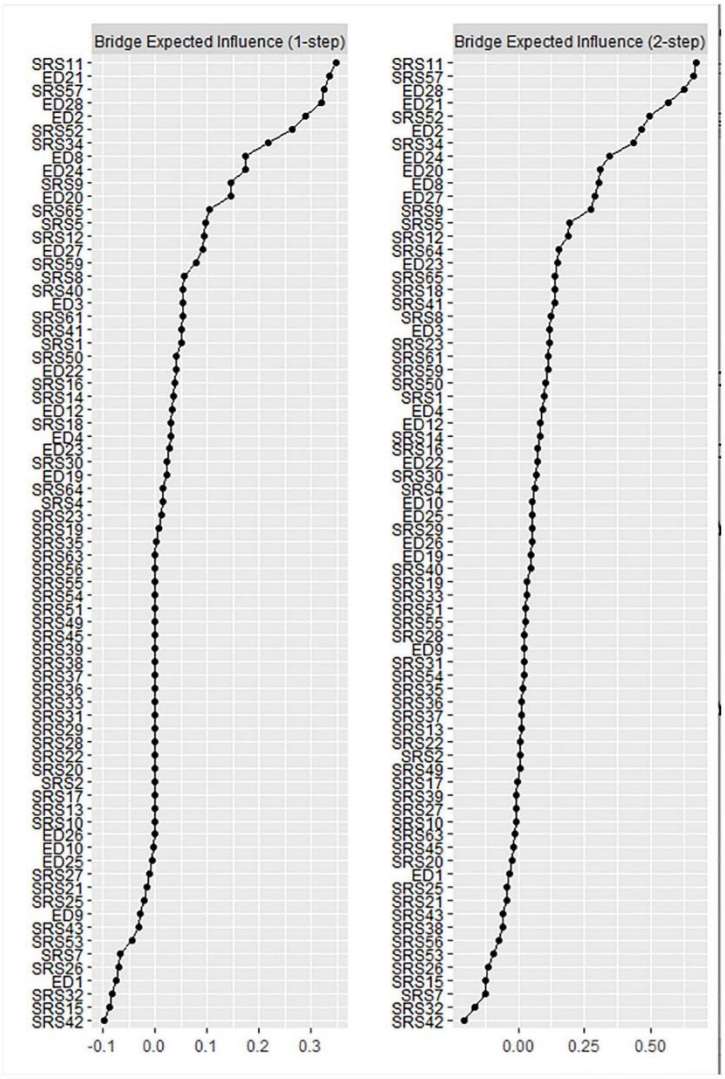

FIGURE 3 | Bridge expected influence (EI) plots. Values are given as Z scores, and higher values indicate more influential nodes in the network.

(33, 49). This might be in part due to AN samples being mostly female, a factor which is associated with lower levels of restricted interests in those with ASD (87). However, there is some evidence to suggest that males and females with ASD show differences in the types of topics they are interested in (e.g., people/animals in females rather than objects/things in males), therefore ASD symptom rating scales may not be sensitive to more female-typical presentations (88) Finally, our study examined relationships between symptoms on a group basis, however an interesting direction for future research would be to construct networks based on an individual basis. It is now possible to examine temporal associations between symptoms within individuals, potentially providing insight into which symptoms may be maintaining psychopathology and therefore

could be targeted during treatment (89). Thus, network analysis could be a useful tool in the move toward more personalized treatments in psychiatry.

Several limitations of the current study should be noted. Our sample size was relatively small given the number of items included in the network, therefore the findings require replications in larger samples. Nonetheless, our stability analyses indicated the centrality indices were stable enough to be interpreted meaningfully. Secondly, only items from self-report questionnaires were considered as nodes in the network. It is likely that vulnerability factors not measured in this study are also important in explaining comorbidity between AN and ASD. For example, given the similarities in neuropsychological profiles, performance on set-shifting or other tests of executive functioning could be included as nodes in comorbidity networks. Although other aspects of psychopathology and social cognition were collected as part of our wider study, these were not included as we wanted to focus on ASD and AN comorbidity specifically, and adding more nodes to the network may have resulted in reductions in the stability and accuracy of the network. Finally, although we confirmed a past or current diagnosis of AN in our sample, we did not confirm whether participants held a diagnosis of ASD. Although scores on the SRS-2 suggested high levels of ASD traits in our sample, there may be qualitative differences in relations between symptoms between individuals with lifetime AN who do and do not have a formal diagnosis of ASD. Previous research suggests around 10% of those with AN meet full diagnostic criteria, and a further 40% display high ASD traits (49). Future studies using a network analytic approach may be useful in establishing which symptoms reflect "true" ASD, and which may be a consequence of starvation.

In conclusion, our results suggest that isolation, difficulties in relating to others, and feelings of tension during social situations may be central symptoms maintaining AN and ASD psychopathology. These symptoms are most strongly connected to other symptoms in the network, and it is suggested that targeting these symptoms in treatment may lead to improvements in the mental health of individuals with past or current AN who also show ASD traits. It must be noted that while central symptoms may be causally influential, longitudinal studies are required to confirm the directionality of relationships between symptoms. We also identified bridge nodes from each disorder cluster; those with the strongest connections to symptoms to the other symptom cluster. Poor self-confidence (ASD cluster), concern around social eating (ED cluster), and concern over other's seeing one's body were (ED cluster) were the strongest bridge symptoms. These symptoms may be important in understanding AN and ASD comorbidity.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by NHS Camberwell St Giles Research Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JK-G contributed to the conception and design of the study. JK-G and DH performed the statistical analysis. JK-G wrote the manuscript. DH, AH, and KT contributed to manuscript revision, read and approved the submitted version. KT lead the research group under which the study took place.

FUNDING

JK-G is supported by a doctoral studentship from the Economic and Social Research Council (ESRC), and received research funding from the Psychiatry Research Trust. AH is funded by the Medical Research Council (MRC) (MR/S020381/1). KT would like to acknowledge: MRC-MRF fund (MR/R004595/1); the Health Foundation, an independent charity committed to bring better health care for people in the UK (1115447); and the Maudsley Charity for their support.

ACKNOWLEDGMENTS

The authors would like to thank the participants who took part in the research for their time.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2020.00401/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

4.1 Supplementary material

R codes

```
#retrieve data file and load library
Data <- read.csv("edeSRS.csv")[-1]
library(qgraph)
library(networktools)
library(bootnet)
View(Data)

#goldbricker
gb_edsrs <- goldbricker(Data, p = 0.05, threshold = 0.25)

#drop bad pairs
reduced_edsrs <- net_reduce(data = Data, badpairs = gb_edsrs,
method="best_goldbricker")

#or combine pairs
reduced_edsrs <- net_reduce(data = Data, badpairs = gb_edsrs)

#save reduced data set
save(reduced_edsrs, file = "reduced_edrs.Rdata")
write.csv(reduced_edsrs, file = "reduced_edrs.csv", row.names=F)

#import reduced data set
reduced_edsrs <- read.csv("reduced_edrs.csv")

#create groups
groups <- list(EDEQ = c(1:18), SRS2 = c(19:73))

#create correlation matrix
cor <-cor_auto(reduced_edsrs)

#create EBIC graph
EBICgraph <-qgraph(cor, graph = "glasso", layout = "spring", labels =
colnames(reduced_edsrs), tuning = 0.25, sampleSize = nrow(reduced_edsrs), groups
= groups)

#save EBIC graph
```

```
EBICgraph <-qgraph(cor, graph = "glasso", layout = "spring", labels =
colnames(reduced_edsrs), tuning = 0.25, sampleSize = nrow(reduced_edsrs), groups
= groups, filetype='png')

#plot expected influence centrality
centralityPlot(EBICgraph, include = "ExpectedInfluence", orderBy =
"ExpectedInfluence")

#plot bridge metrics
b <-  bridge(EBICgraph, communities = groups)
plot(b, order = "value", include = c("Bridge Expected Influence (1-step)", "Bridge
Expected Influence (2-step)"))

#Estimates network for bootstrapping
Network_reduced <- estimateNetwork(reduced_edsrs, default = 'cor')

#Bootstraps, nonparametric
Results_bridge_ei_nonparameteric <- bootnet(Network_reduced,
default='EBICglasso', type='nonparametric',
                nBoots = 1000, nCores = 8, statistics = c('bridgeExpectedInfluence',
'edge', 'strength', 'expectedInfluence'))

#Plot bootstrapped edge CIs:
plot(Results_bridge_ei_nonparameteric, labels = TRUE, order = 'sample',statistics =
'edge')

#Plot significant differences (alpha = 0.05) of edges, expected influence, expected
bridge influence:
plot(Results_bridge_ei_nonparameteric, "edge", plot = "difference",onlyNonZero =
TRUE,
    order = "sample")
 plot(Results_bridge_ei_nonparameteric, "expectedInfluence", plot = "difference")
plot(Results_bridge_ei_nonparameteric, " 'bridgeExpectedInfluence'", plot =
"difference")


#Case-drop bootstrap. This is needed to compute cs-coefficients and stability
Results_case_bridge_ei <- bootnet(Network_reduced, nBoots = 2000, nCores = 10,
                type = "case", default='EBICglasso', statistics =
c('bridgeExpectedInfluence', 'edge', 'strength',  'expectedInfluence'))
```

```
#Plot centrality stability:
plot(Results_case_bridge_ei, statistics =
c('bridgeExpectedInfluence','expectedInfluence',))

#Compute CS-coefficients:
corStability(Results_case_bridge_ei)
```

Supplementary table 1. Scale items

Eating Disorder Examination Questionnaire (EDE-Q)	1. Have you been deliberately trying to limit the amount of food you eat to influence your shape or weight (whether or not you have succeeded)? 2. Have you gone for long periods of time (8 waking hours or more) without eating anything at all in order to influence your shape or weight? 3. Have you tried to exclude from your diet any foods that you like in order to influence your shape or weight (whether or not you have succeeded)? 4. Have you tried to follow definite rules regarding your eating (for example, a calorie limit) in order to influence your shape or weight (whether or not you have succeeded? 5. Have you had a definite desire to have any empty stomach with the aim of influencing your shape or weight?† 6. Have you had a definite desire to have a totally flat stomach?† 7. Has thinking about food, eating, or calories made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?† 8. Has thinking about shape or weight made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)? 9. Have you had a definite fear of losing control over eating? 10. Have you had a definite fear that you might gain weight? 11. Have you felt fat?† 12. Have you had a strong desire to lose weight? 13. Over the past 28 days, how many times have you eaten what other people would regard as an unusually large amount of food (given the

	circumstances)? ††
	14. …On how many of these times did you have a sense of having lost
	control over your eating (at the time that you were eating)? ††
	15. Over the past 28 days, how many DAYS have such episodes of
	overeating occurred (i.e., you have eaten an unusually large amount of
	food and have had a sense of loss of control at the time)? ††
	16. Over the past 28 days, how many times have you made yourself sick
	(vomit) as a means of controlling your shape or weight? ††
	17. Over the past 28 days, how many times have you taken laxatives as a
	means of controlling your shape or weight? ††
	18. Over the past 28 days, how many times have you exercised in a
	“driven” or “compulsive” way as a means of controlling your weight,
	shape, or amount of fat, or to burn off calories? ††
	19. Over the past 28 days, on how many days have you eaten in secret (i.e., furtively)?
	20. On what proportion of the times that you have eaten have you felt guilty (felt that you’ve done wrong) because of its effect on your shape or weight?
	21. Over the past 28 days, how concerned have you been about other people seeing you eat?
	22. Has your weight influenced how you think about (judge) yourself as a person?
	23. Has your shape influenced how you think about (judge) yourself as a person?
	24. How much would it have upset you if you had been asked to weigh yourself once a week (no more, or less, often) for the next four weeks?
	25. How dissatisfied have you been with your weight?
	26. How dissatisfied have you been with your shape?

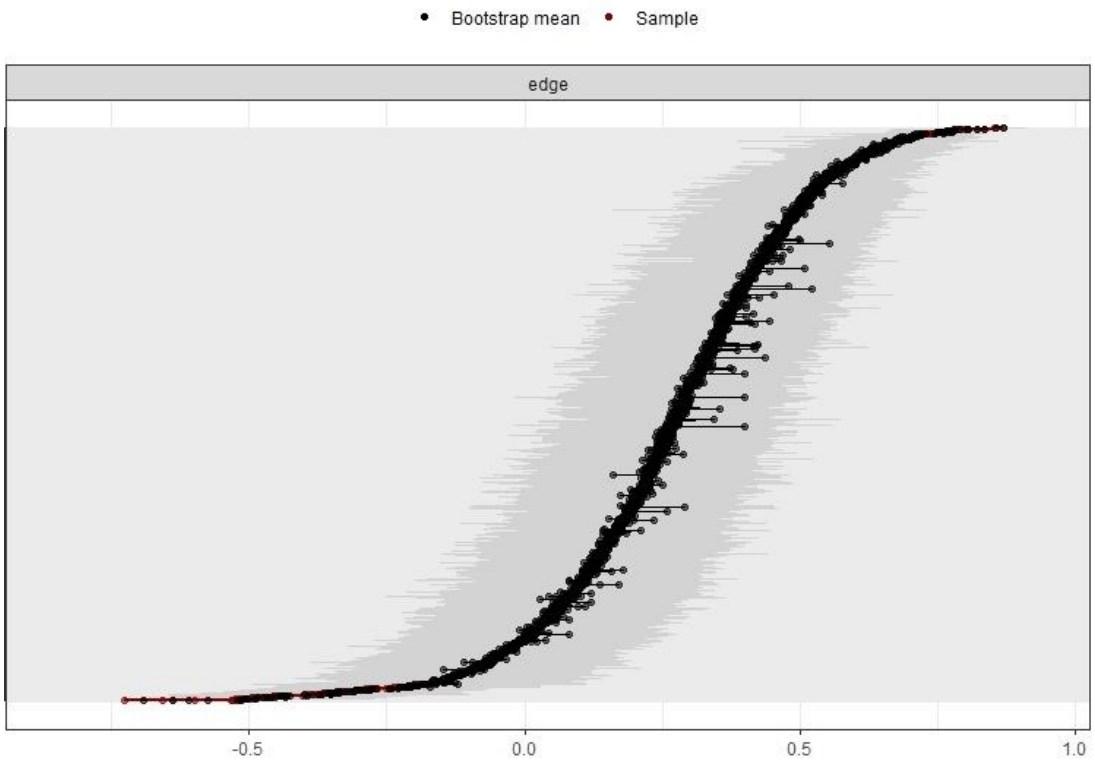
	27. How uncomfortable have you felt seeing your body (for example, seeing your shape in the mirror, in a shop window reflection, while undressing or taking a bath or shower)? 28. How uncomfortable have you felt about others seeing your shape or figure (for example, in communal changing rooms, when swimming, or wearing tight clothes?
Social Responsiveness Scale, adult self-report version (SRS-2)	1. I am much more uncomfortable in social situations than when I am by myself. 2. My facial expressions send the wrong message to others about how I actually feel. 3. I feel self-confident when interacting with others.† 4. When under stress, I engage in rigid or inflexible patterns of behaviour that seem odd to people. 5. I do not recognize when others are trying to take advantage of me.† 6. I would rather be alone than with others. 7. I am usually aware of how others are feeling. 8. I behave in ways that seem strange or bizarre to others. 9. I am overly dependent on others for help with meeting my everyday needs. 10. I take things too literally, and because of that, I misinterpret the intended meaning of parts of a conversation. 11. I have good self-confidence. 12. I am able to communicate my feelings to others. 13. I am awkward in turn taking interactions with others (for example, I have a hard time keeping up with the give-and-take of a conversation. 14. I am not well coordinated. 15. When people change their tone or facial expression, I usually pick up on that and understand what it means. 16. I avoid eye contact or am told that I have unusual eye contact. 17. I recognise when something is unfair. 18. I have difficulty making friends, even when I'm trying my best. 19. I get frustrated trying to get ideas across in conversations.

	20. I have sensory interests that others find unusual (for example, smelling or looking at things in a special way). 21. I am able to imitate others' actions and expressions when it is socially acceptable to do so. 22. I interact appropriately with other adults. 23. I do not join group activities or social events unless prompted or strongly urged to do so. 24. I have more difficulty than others with changes in my routine.† 25. I do not mind being out of step with or "not on the same wavelength" as others. 26. I offer comfort to others when they are sad. 27. I avoid starting social interactions with other adults. 28. I think or talk about the same thing over and over. 29. I am regarded by others as odd or weird. 30. I become upset in situations with lots of things going on. 31. I can't get my mind off something once I started thinking about it. 32. I have good personal hygiene. 33. My behaviour is socially awkward, even when I'm trying to be polite. 34. I avoid people who want to be emotionally close to me. 35. I have trouble keeping up with the flow of normal conversation. 36. I have difficulty relating to family members. 37. I have difficulty relating to adults outside of my family. 38. I respond appropriately to mood changes in others (for example, when a friend's mood changes from happy to sad). 39. People think I am interested in too few topics, or that I get carried away with those topics. 40. I am imaginative. 41. I sometimes seem to wander aimlessly from one activity to another. 42. I am overly sensitive to certain sounds, textures, or smells. 43. I enjoy small talk (casual conversation with others).

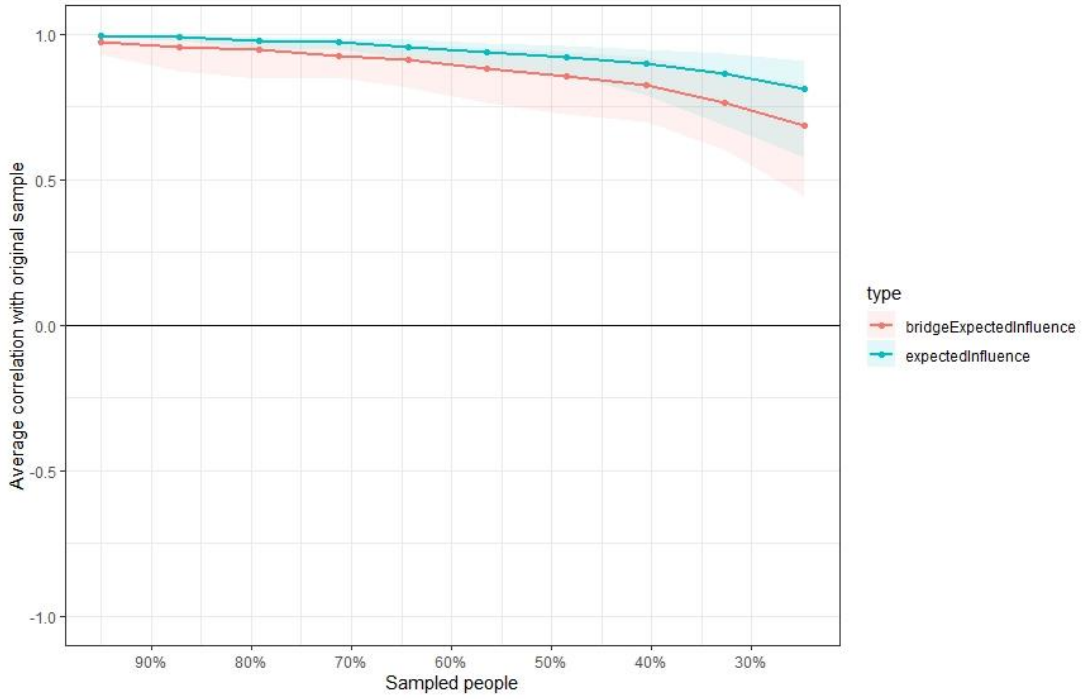
	44. I have more trouble than most people with understanding chains of causation (in other words, how events are related to one another).†
	45. When others around me are paying attention to something, I get interested in what they are attending to.
	46. Others feel that I have overly serious facial expressions.†
	47. I laugh at inappropriate times.†
	48. I have a good sense of humor and can understand jokes.†
	49. I do extremely well at certain kinds of intellectual tasks, but do not do as well at most other tasks.
	50. I have repetitive behaviours that others consider odd.
	51. I have difficulty answering questions directly and end up talking around the subject.
	52. I get overly loud without realizing it.
	53. I tend to talk in a monotone voice (in other words, less inflection of voice than most people demonstrate).
	54. I tend to think about people in the same way I do objects.
	55. I get too close to others of invade their personal space without realizing it.
	56. I sometimes make the mistake of walking between two people who are trying to talk to one another.
	57. I tend to isolate myself.
	58. I concentrate too much on parts of things rather than seeing the whole picture.†
	59. I am more suspicious than most people.
	60. Other people think I am emotionally distant and do not show my feelings.†
	61. I tend to be inflexible.
	62. When I tell someone my reason for doing something, it strikes the person as unusual or illogical.†
	63. My way of greeting another person is unusual.
	64. I am much more tense in social settings than when I am by myself.
	65. I find myself staring or gazing off into space.

†Item was removed by goldbricker

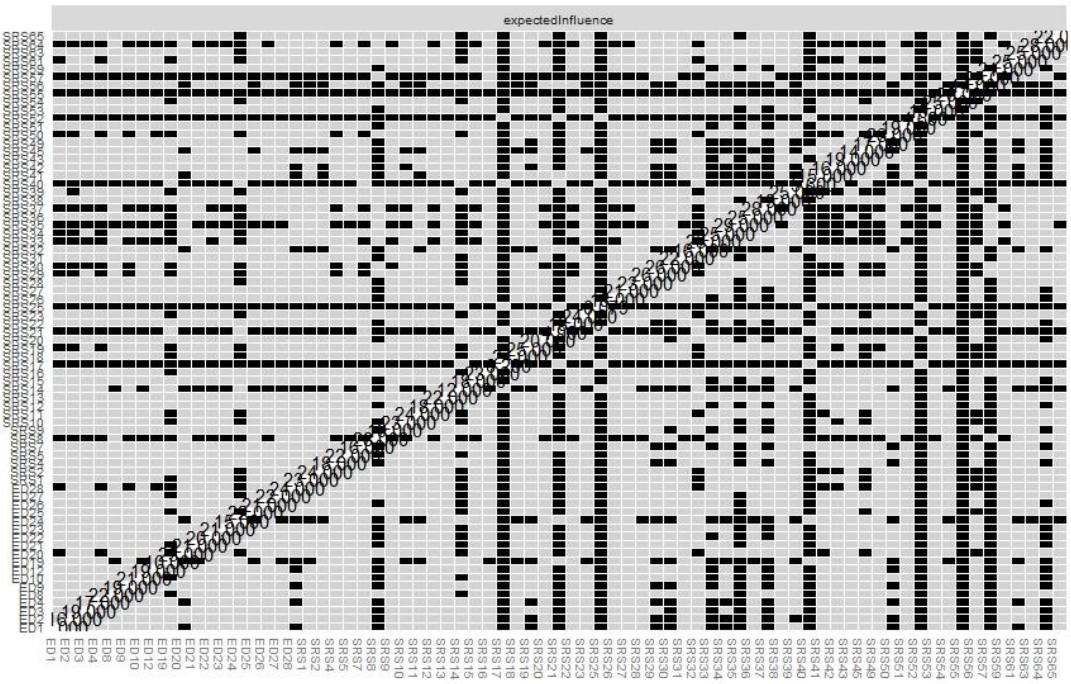
††Frequency item not included



Supplementary figure 1. Bootstrapped confidence intervals (CIs, grey areas) of estimated edge weights. Each horizontal line represents an edge in the network, ordered from the edge with the highest weight to the edge with weight. y-axis labels have been removed to avoid cluttering.



Supplementary figure 2. Bootstrapped expected influence and bridge expected influence stability. Solid lines indicate centrality correlation coefficients, shaded areas are 95% confidence intervals.



Supplementary figure 3. Bootstrapped difference tests between symptoms in the network. Black boxes indicate a significant difference in expected influence centrality between two symptoms, grey boxes represent nonsignificant differences.

Supplementary figure 4. Bootstrapped difference tests between symptoms in the network. Black boxes indicate a significant difference in bridge expected influence between two symptoms, grey boxes represent nonsignificant differences.

Chapter 5 - Self-reported autistic traits mediate reductions in social attention in adults with anorexia nervosa

5.1 Introduction

Anorexia nervosa (AN) is a severe psychiatric disorder characterised by an intense fear of gaining weight, persistent behaviour to restrict energy intake, and disturbances in the way one's body or shape is experienced (American Psychiatric Association [APA], 2013). AN is associated with high levels of psychiatric comorbidity. For example, recent research suggests that between 4 and 52.5% of individuals with AN show clinically significant levels of autism spectrum disorder (ASD) symptoms, scoring above clinical cut-offs on assessment tools such as the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) (Westwood et al., 2018; Westwood & Tchanturia, 2017). The presence of ASD symptoms in individuals with AN has been associated with more frequent and longer inpatient stays (Nazar et al., 2018), poorer outcomes (Anckarsäter et al., 2012; Nielsen et al., 2015; Wentz et al., 2009), and less improvement during treatment (Stewart et al., 2017; Tchanturia et al., 2016). At the same time, individuals with ASD are at greater risk of developing eating disorder symptoms than non-autistic people (Nickel et al., 2019; Solmi et al., 2020). Around a quarter of women with ASD report clinically significant levels of eating disorder symptoms (Spek et al., 2019), and adults with ASD are more likely to be in non-healthy weight categories (underweight, overweight, or obese) than non-autistic people (Sedgewick et al., 2020)

Contemporary models of AN emphasise interpersonal difficulties as key factors in the development and maintenance of the disorder (Fairburn et al., 2003; Treasure & Schmidt, 2013). During the illness, individuals with AN show high levels of social anhedonia (reduced interest or pleasure from social situations) and social anxiety, difficulties that persist after recovery (Harrison et al., 2014; Kerr-Gaffney et al., 2018; Tchanturia, Davies, Harrison, et al., 2012). Individuals with AN also report poorer social skills, and use fewer positive social problem-solving strategies compared to healthy controls (HCs) (Rhind et al., 2014; Sternheim et al., 2012). Further, research has documented lower levels of social support, reduced social networks, and high levels of isolation in those with AN (Adenzato et al., 2012; Arkell & Robinson, 2008; Doris et al., 2014; Gillberg et al., 1994; Tiller et al., 1997). Importantly, there is

evidence to suggest that social difficulties may be present before illness onset. Up to two thirds of individuals with AN report having early social difficulties, and are more likely to report having no childhood friends and a history of being bullied than their unaffected peers (Cardi, Mallorqui-Bague, et al., 2018; Fairburn et al., 1999; Gillberg & Råstam, 1992; Lie et al., 2019). Given that interpersonal problems are associated with poorer outcomes in those with AN (Franko et al., 2013; Zipfel et al., 2000), it is important to understand possible underlying cognitive mechanisms.

Attending to others' eye gaze, facial expressions, posture, and gestures is key to effective social interaction, as these nonverbal cues convey important information about an individual's emotions, thoughts, and intentions. In typical human development, social information is highly salient, with infants as young as a few days old showing a preference for face stimuli (Reynolds & Roth, 2018). Indeed, reductions in social attention are among the first characteristics of disorders of social communication such as ASD (Jones et al., 2014). Reduced attention to faces, and particularly the eyes, has been found to predict degree of social impairment and emotion recognition in those with ASD (Corden et al., 2008; Falkmer et al., 2011; Klin et al., 2002; Müller et al., 2016). Differences in social attention have also been found in individuals with social anxiety disorder, where avoidance of eye contact and other social gestures are hypothesised to act as safety behaviours. Such behaviours are an attempt to reduce anxiety or prevent a feared negative event, but perpetuate anxiety in the long term. As a result of this reduction in attention to social information, fears around social evaluation are prevented from being disconfirmed, and positive social experiences are not registered, thereby maintaining the disorder (Chen & Clarke, 2017).

It is possible then, that differences in social attention might relate to interpersonal difficulties associated with AN. However, much less research has examined social attention in this population. Several studies have used the pictorial Stroop or dot-probe task, reporting an attentional bias towards angry and rejecting faces and away from neutral and compassionate facial expressions in individuals with AN (Cardi et al., 2012; Cardi, Matteo, et al., 2014; Harrison, Sullivan, et al., 2010). However, these reaction time (RT) based paradigms have a number of limitations. For example,

increased RTs to faces in the emotional Stroop task are interpreted as increased attention, as the emotional salience of the face interferes with one's response latency. However, it is equally possible that participants diverted their attention away from the stimulus, thereby increasing RTs (Aspen et al., 2013). Further, these tasks use isolated static faces, and are therefore unable to provide much insight into attention to social information in real life, dynamic environments, as well as potential differences in attention to facial features.

A few studies have therefore used eye-tracking paradigms to directly capture attention to social stimuli in AN. For example, Pinhas et al. (2014) found that participants with AN payed less attention to images of social interactions when presented alongside images of body shapes, whereas HCs spent similar amounts of time looking at both types of image. Similarly, Watson et al. (2010) found that a small group of weight-restored AN spent less time looking at faces when the body was also present within the image, compared to HCs. Importantly, when faces were presented alone, participants with AN looked significantly less at the eyes than HCs, providing the first eye-tracking evidence of abnormal social attention in the absence of disorder-relevant body stimuli. This finding was replicated in a study by Harrison et al. (2019), who found reduced attention to the eyes of both static face images, videos of social interactions, and during a real-life social interaction in acute AN compared to recovered AN and HCs. Similar to findings in ASD, reduced attention to the eyes was associated with greater self-reported social difficulties. In summary, there is preliminary evidence to support reduced attention to social information, and particularly the eyes, in individuals with AN.

Thus far, studies using dynamic stimuli have not measured attention to other parts of the face, such as the nose and mouth, in individuals with AN. Although areas such as the nose may convey less information about emotions or other mental states, eye-tracking research has shown that healthy individuals generally shift between looking at the eyes, nose, and mouth during both free viewing and face recognition tasks (Hsiao & Cottrell, 2008; Vo et al., 2012; Walker-Smith et al., 1977). In addition, research in individuals with ASD has shown that increased attention to the mouth is associated with better social adjustment, suggesting that those with ASD may employ

compensatory strategies to derive meaning from other parts of the face, differently from HCs (Klin et al., 2002). The findings from ASD are particularly important for the study of social attention in individuals with AN, given the emerging literature documenting comorbidity between the two conditions (Westwood et al., 2018).

Thus, the primary aim of the current study was to examine attention to faces, as well as core facial features (eyes, nose, mouth), while viewing a naturalistic, dynamic social scene in individuals with AN, recovered AN, and HCs. It was hypothesised that individuals with acute AN would spend less time looking at faces and eyes of faces compared to HCs. We predicted intermediate levels of attention in those recovered from AN. A second aim was to examine whether ASD traits were associated with social attention. Further, given that AN is also associated with high levels of depression (Godart et al., 2015), anxiety (Kerr-Gaffney et al., 2018; Swinbourne & Touyz, 2007), and alexithymia (Westwood, Kerr-Gaffney, et al., 2017), factors which may themselves alter socio-cognitive processes (Claudino et al., 2019; Duque & Vázquez, 2015; Frazier et al., 2017; Fujiwara, 2018; Gregory et al., 2019), a third aim was to examine whether comorbid psychopathology was associated with social attention. It was hypothesised that high levels of ASD traits would be associated with less time spent looking at faces and eyes, as well as a longer delay until first fixation on the face.

5.2 Methods

5.2.1 Participants

Ethical approval was obtained from the National Health Service (NHS) Research Ethics Committee (Camberwell St Giles, 17/LO/1960). All participants were required to be between 18 and 55 years old and fluent in English. Exclusion criteria were a history of brain trauma or learning disability. HC participants were recruited through a King's College London email circular and posters around campuses. Before taking part, HC participants were screened using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV; First et al., 2015), to ensure they did not show

symptoms consistent with any psychiatric disorders. In addition, HCs were required to have a body mass index (BMI) between 19 and 27.

In addition to the university advertisements, participants with current or past AN were recruited through online advertisements (B-eat, call for participants, MQ mental health) and through two specialist eating disorder services in London. Participants were interviewed with the SCID-5-RV to confirm a current or past diagnosis of AN. Participants with AN were required to have a BMI ≤ 18.5, and recovered participants a BMI between 19 and 27.

5.2.2 Materials

The eye-tracking stimulus material was a movie clip from the Dynamic Images and Eye Movements database ("Fifty People One Question: Brooklyn", http://thediemproject.wordpress. com/), in which several pedestrians in Brooklyn, New York are interviewed and are seen speaking to the camera. The original audio accompanying the clip was replaced with background music, in order to control for the effects of speech comprehension on attention (Vo et al., 2012). The clip was chosen for its depiction of what would typically be seen when engaging in a natural social interaction with one or two people, as well as its lack of body information (people were seen from the shoulders up), as this is known to be a salient class of stimuli in individuals with AN (Pinhas et al., 2014). The clip lasted 42s, and participants were asked to simply view the clip as they would watch television. Total looking times (in seconds) to the screen were computed to control for overall attention to the stimulus, and total fixation duration to each area of interest (AOI) was calculated (as a proportion of total valid samples).

Figure 1 depicts a single frame from the video, depicting the AOIs of interest (whole face, eyes, nose, and mouth). Note that the face AOI included the core features as well as the outer regions of the face. AOIs were drawn on each individual frame of the video using Apple Motion (Apple, 2019). Core feature AOIs encompassed the features, but also extended outward to include emotionally expressive regions that border the features themselves (e.g., the eye region includes the eyebrows). Face

AOIs followed the outline of the face, starting just below the hairline and following along the jawline.

Figure 1. A single frame from the video clip “Fifty People, One Question: Brooklyn” (left), and with the areas of interest (AOIs) overlaid (right).

To capture attention to faces, two dependent measures were used: fixation duration to face AOIs, and time to first fixation on the face. To capture attention to core facial features, the following dependent measures were used: fixation duration to eye, nose, and mouth AOIs, and eye-to-mouth viewing ratio, defined as fixation duration on eyes/(fixation duration on eyes + fixation duration on mouth).

The Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2, Lord et al., 2012) is a standardised semi-structured interview for the assessment of ASD. It includes a range of questions and activities designed to evoke behaviours and cognitions associated with ASD. The revised algorithm, which was designed to more closely reflect the DSM-5 criteria for ASD was used for scoring (Hus & Lord, 2014). The algorithm has two subscales: social affect and restrictive and repetitive behaviours, and total scores of 8 or more indicate possible ASD.

The Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II; Wechsler, 2011) was used to measure IQ, to ensure groups were matched in this respect. The two subtest version was used (vocabulary and matrix reasoning).

5.2.2.1 Self-report questionnaires

The Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994) measures severity of eating disorder symptoms, with higher scores indicating more severe psychopathology. The EDE-Q consists of 28 items, 22 of which are rated on a 7-point Likert scale. Total scores (range: 0-6) are calculated by averaging responses

across these items. The scale also includes six items assessing frequency of various eating disorder behaviours, but responses can take on any value and are not included in total score calculations. HCs with a score of ≥2.7 were excluded from analyses to ensure those with sub-threshold eating disorder symptoms were not included (Lang, Larsson, et al., 2016; Mond et al., 2004, 2006). Cronbach's alpha was 0.93.

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) is a 14-item questionnaire with two subscales measuring severity of anxiety and depression. Subscale scores are interpreted as: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21). Cronbach's alpha was 0.93.

The Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987) is a 48-item questionnaire assessing severity of social anxiety symptoms. Total scores range from 0 to 144, and a score of 60 or more has been established as a cut-off indicative of social anxiety disorder (Rytwinski et al., 2009). Cronbach's alpha was 0.97.

The twenty-item Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994) measures severity of alexithymia, with three subscales: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. Total scores range from 0 to 100, and cut-offs are as follows: ≤51 = no alexithymia; 52-60 = borderline alexithymia; and ≥61 = alexithymia (Parker et al., 1993). Cronbach's alpha was 0.91.

The Social Responsiveness Scale-2nd Edition, adult self-report form (SRS-2; Constantino & Gruber, 2012) includes five subscales, measuring symptoms associated with ASD: social awareness, social cognition, social communication, social motivation, and restricted and repetitive interests. SRS-2 scores have been shown to be associated with functional impairment in individuals with AN, however scores are independent from indicators of malnutrition such as BMI and illness duration (Kerr-Gaffney et al., 2020). Cronbach's alpha was 0.96.

The Work and Social Adjustment Scale (WSAS; Mundt et al., 2002) is a brief measure of functional impairment in five domains: work, home management, social leisure, private leisure, and ability to form and maintain close relationships. Scores range

from 0 to 40, with a score of 20 or more indicating clinical significance. Cronbach's alpha was 0.92.

5.2.3 Procedure

Participants attended a testing session at the Institute of Psychiatry, Psychology & Neuroscience. After written informed consent was obtained, participants viewed the video clip while their eye movements were recorded using a Tobii TX300 eye-tracker. The desktop mounted eye-tracker had a sampling rate of 300Hz, a screen resolution of 1920 x 1080, and a diagonal screen size of 23". During tracking, infrared diodes generate reflections on the participant's retinas and corneas. From this reflection, the angular rotation of each eye is estimated. Before stimulus presentation, a 5-point calibration procedure was run. Calibration relates the angular rotation of each eye to the corresponding x and y coordinates on the screen surface. Participants were seated approximately 60cm from the screen. Stimulus presentation, behavioural data, and eye-tracking data were managed and recorded using custom-written Matlab software (Mason, 2015, https://sites.google.com/site/taskenginedoc).

After eye-tracking, the first author administered the WASI-II and the ADOS-2, and the participant completed the questionnaires. Weight and height measurements were taken to calculate BMI (weight/height^2). Participants were reimbursed £20 for their time.

5.2.4 Analysis

Histograms and Q-Q plots were inspected to check for normal distributions. Where variables were positively skewed (as was the case for age and time to first fixation to the face), a logarithmic transformation was applied for analyses, however original values (*M* and *SD*) are reported for clarity. Homogeneity of variances were assessed using Levene's test. Group differences in psychopathology, demographic information, and attention outcome measures were assessed using one-way ANOVAs (or Welch's ANOVA with Games-Howell post-hoc tests where the assumption of homogeneity was violated), with the exception of attention to core feature AOIs, which was assessed using a mixed ANOVA. Independent samples *t*-tests were used

when assessing group differences between AN and REC only, and to test for differences between medicated and unmedicated participants. Chi-squared tests of homogeneity (or Fisher's exact test where the sample size assumption was not met) were conducted for dichotomous variables.

To examine associations between psychopathology and attention, Spearman's correlations between attention variables, psychopathology, and selected demographic variables were run. Where significant correlations were found, variables were entered into hierarchical linear regressions to determine whether dimensions of psychopathology predicted social attention, over and above group membership. Assumptions for hierarchical regressions were assessed with partial regression plots, and plots of studentized residuals against predicted values. Independence of residuals was assessed using the Durbin-Watson statistic, and outliers with studentised deleted residuals greater than ±3 were excluded from analyses.

The SPSS macro PROCESS (Hayes, 2017) was used for mediation analyses. PROCESS generates bias-corrected 95% bootstrap confidence intervals (CIs) for the indirect effect (based on 5000 samples), and is more powerful than the causal steps approach to mediation (Hayes & Preacher, 2014).

5.3 Results

5.3.1 Demographics

In total, 148 participants were recruited (46 AN, 51 REC, 51 HC). Five HCs were subsequently excluded based on their EDE-Q scores and one REC participant was excluded due to a BMI >27. A further 13 participants were excluded from analyses due to: eye-tracking equipment failure on the day of testing (*n* = 2), low quality eye-tracking data, defined as a proportion of valid samples of less than 0.25 (*n* = 9), outliers identified with residuals more than 3 SDs from the mean (*n* = 2). Thus, data from 129 participants were included in analyses, demographic and clinical information for which is presented in Table 1. Groups were similar in age, sex, years

of education received, and IQ. Participants in the REC group had been recovered for an average of 4.44 years (*SD* = 4.46).

Table 1. Mean (*SD*) demographic information and psychopathology scores

	AN (*N* = 41)	REC (*N* = 48)	HC (*N* = 40)	Test statistics	*p*-value	ηp²/*d*
Age (years)[†]	26.66 (8.59)	26.10 (8.15)	23.90 (4.75)	*F*(2, 80.76) = 1.63	.203	.02
% female	90.2	97.9	95.0	Fisher's exact test = 2.39	.295	
BMI	15.81 (1.37)[a]	21.18 (1.91)[b]	21.75 (1.96)[b]	*F*(2, 125) = 142.10	**<.001**	.70
Years of education	16.21 (3.10)	16.58 (2.62)	16.42 (2.41)	*F*(2, 125) = 0.20	.822	.00
IQ	110.00 (12.21)	110.44 (10.75)	113.46 (7.05)	*F*(2, 80.09) = 1.88	.159	.02
Age diagnosed[†]	19.78 (6.77)[a]	16.36 (3.59)[b]	-	*t*(59.53) = 2.89	**.005**	.63
Illness length (years)	6.87 (7.80)	5.48 (5.69)	-	*t*(72.65) = 0.94	.353	.20
% on psychiatric medication	48.8	31.3	-	X^2 = 2.85	.091	
ADOS-2						
Total	4.68 (4.10)[a]	4.23 (4.53)[ab]	2.58 (2.45)[b]	*F*(2, 79.79) = 5.03	**.009**	.05
% above clinical cut-off	19.5[a]	25.0[a]	2.5[b]	X^2 = 8.57	**.014**	
EDE-Q	3.79 (1.27)[a]	1.82 (1.53)[b]	0.50 (0.46)[c]	*F*(2, 67.14) = 125.46	**<.001**	.55
HADS-A	13.24 (4.53)[a]	10.83 (5.16)[a]	4.73 (2.82)[b]	*F*(2, 80.33) = 61.11	**<.001**	.40

HADS-D	9.46 (4.19)[a]	5.02 (4.06)[b]	1.50 (1.72)[c]	$F(2, 73.40) = 69.21$	**<.001**	.45
LSAS	69.18 (28.53)[a]	57.17 (30.29)[a]	27.00 (17.80)[b]	$F(2, 79.65) = 37.92$	**<.001**	.30
SRS-2	79.98 (30.97)[a]	70.19 (32.30)[a]	36.45 (17.26)[b]	$F(2, 77.72) = 39.03$	**<.001**	.30
TAS-20	57.75 (13.76)[a]	49.81 (15.08)[b]	36.00 (9.97)[c]	$F(2, 81.26) = 35.21$	**<.001**	.31
WSAS	21.93 (8.62)[a]	11.27 (8.74)[b]	2.75 (5.20)[c]	$F(2, 80.42) = 75.83$	**<.001**	.50

ADOS-2, Autism Diagnostic Observation Schedule, 2nd edition; AN, anorexia nervosa; BMI, body mass index; EDE-Q, eating disorder examination questionnaire; HADS-A, hospital anxiety and depression scale, anxiety subscale; HADS-D, hospital anxiety and depression scale, depression subscale; HC, healthy control; IQ, intelligence quotient; LSAS, Liebowitz social anxiety scale; REC, recovered anorexia nervosa; SD, standard deviation; SRS-2, social responsiveness scale, 2nd edition; TAS-20, twenty-item Toronto alexithymia scale

Different superscripts indicate significant differences between groups, significant *p*-values are highlighted in bold. Psychopathology scores reflect total scores unless otherwise stated.

[†]Variable was log transformed for analyses, original values are displayed.

5.3.2 Attention to faces

There were no significant differences between groups in time spent looking at the screen, $X^2(2) = 1.08$, $p = .581$, indicating the groups did not differ in overall attention to the stimulus. A one-way ANOVA indicated a significant difference in time spent looking at faces, $F(2, 126) = 4.17$, $p = .018$, $\eta p^2 = .06$. Post-hoc analyses indicated that individuals with AN looked at faces significantly less ($M = 0.70$, $SD = 0.12$) than REC ($M = 0.75$, $SD = 0.07$), $p = .050$, and HCs ($M = 0.76$, $SD = 0.07$), $p = .025$, as shown in Figure 2. Regarding time to first fixation, a one-way ANOVA indicated there were no significant differences between individuals with AN ($M = 0.81$s, $SD = 0.50$), REC ($M = 0.76$s, $SD = 0.28$s), or HCs ($M = 0.88$s, $SD = 0.68$s), $F(2, 126) = 0.21$, $p = .81$, $\eta p^2 = .00$.

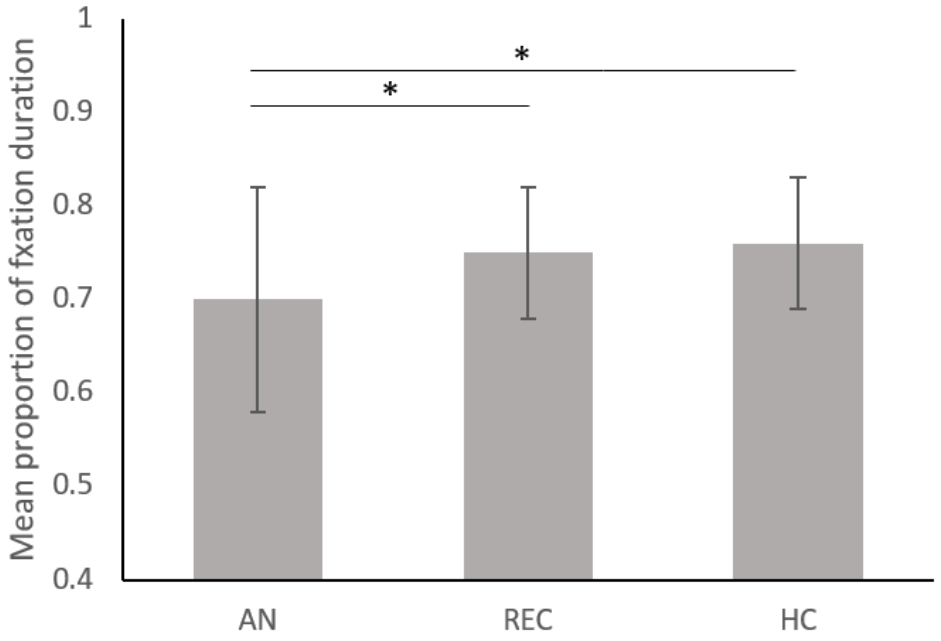


Figure 2. Mean proportion of time spent looking at face AOIs across groups. Error bars represent standard deviation. Significant *p*-values indicating group differences are marked with an asterisk, * < .05. AN = anorexia nervosa; HC = healthy control; REC = recovered anorexia nervosa

5.3.3 Attention to facial features

To examine whether patterns of attention to the different facial features differed between groups, a mixed ANOVA with AOI as the within-subjects factor (eyes, mouth,

and nose) and group as the between-subjects factor was run. A Greenhouse-Geisser correction was applied due to violation of Mauchly's test of sphericity. The interaction between group and AOI was not significant, $F(2.86, 180.13) = 0.96$, $p = .41$, $\eta p^2 = .02$. The main effect of AOI showed a significant difference in proportion of time spent looking at the different facial features, $F(1.43, 180.13) = 11.98$, $p < .001$, $\eta p^2 = .09$. Participants spent significantly more time looking at the eyes than the mouth ($p = .016$) and nose ($p < .001$), as shown in Figure 3. The main effect of group was also significant, $F(2, 126) = 6.47$, $p = .002$, $\eta p^2 = .09$. Post-hoc tests indicated that individuals with AN looked at facial features less than REC ($p = .007$) and HCs ($p = .005$).

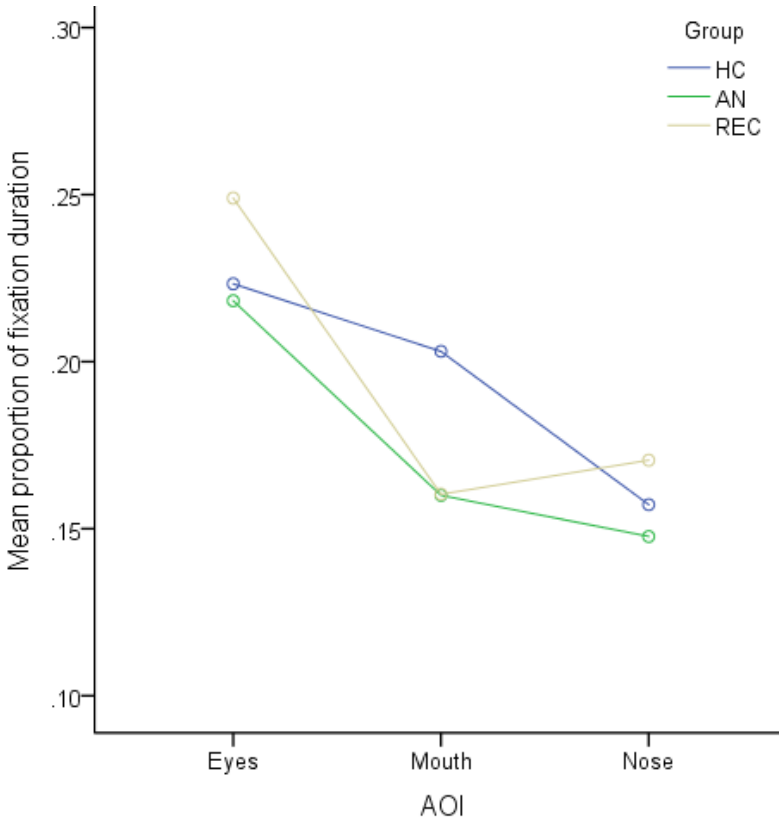


Figure 3. Mean proportion of time spent looking at core facial features across groups. AOI = area of interest; AN = anorexia nervosa; HC = healthy control; REC = recovered anorexia nervosa

Further, a one-way ANOVA indicated there were no significant differences in eye-to-mouth viewing ratio between individuals with AN (M = 0.59, SD = 0.26), REC (M = 0.61, SD = 0.25), and HC (M = 0.53, SD = 0.27), $F(2, 126) = 1.25$, $p = .289$, $\eta p^2 = .02$.

5.3.4 Relationships between social attention and psychopathology

Spearman's correlations between attention variables (time spent looking at faces and core facial feature AOIs, time to first fixation to the face, eye-to-mouth viewing ratio), age, BMI, psychopathology scores (EDE-Q, HADS anxiety, HADS depression, TAS-20, LSAS, SRS-2), and functional impairment (WSAS scores) were run separately for each group, as shown in Table 2. Given that significant correlations would be followed up with regression analyses, they were treated as exploratory and not corrected for multiple comparisons. In individuals with AN, time spent looking at faces was significantly negatively correlated with TAS-20 (r = -.33, p = .040) and SRS-2 scores (r = -.40, p = .011), while time to first fixation to the face was significantly positively correlated with WSAS (r = .37, p = .017), depression (r = .43, p = .006), and anxiety scores (r = .34, p = .031). Time to first fixation on the face was significantly positively correlated with ADOS-2 total scores in HCs (r = .42, p = .007). No significant correlations were found in the REC group.

Given the association between SRS-2 and TAS-20 scores and time spent looking at faces in individuals with AN, a hierarchical regression was run to examine whether SRS-2 and TAS-20 scores predicted time spent looking at faces, above the effects of group. Details of each regression model are presented in table 3. The final model (model 3) was significant, $R^2 = .10$, $F(4, 123) = 3.46$, $p = .010$, adjusted $R^2 = .07$. The addition of SRS-2 scores led to a significant increase in R^2 (model 3), whereas the addition of TAS-20 scores did not (model 2). In the final model, only SRS-2 scores made a significant unique contribution to explaining the variance in time spent looking at faces. This suggests that ASD symptoms predicted looking duration to faces over and above diagnosis, with higher SRS-2 scores being associated with less attention to faces.

Table 2. Spearman's correlations between attention, demographic variables, and psychopathology

AN	Age	BMI	EDE-Q	HADS-A	HADS-D	LSAS	TAS-20	SRS-2	ADOS-2	WSAS
AOI face	.01	.22	-.29	-.21	-.25	-.20	**-.33**	**-.40**	-.23	-.11
AOI eyes	.01	.23	-.22	-.01	-.20	-.07	-.14	-.04	-.31	-.18
AOI mouth	.12	.04	.09	-.28	-.07	.04	-.03	-.25	-.13	-.05
AOI nose	-.05	.12	-.09	.13	.13	.03	.01	.03	.04	.03
Time to first fixation (face)	.07	-.26	.10	**.34**	**.43**	.19	.15	.16	.12	**.37**
Eye-to-mouth viewing ratio	-.14	.08	-.15	.22	.01	-.07	.00	.22	.03	.01
REC	Age	BMI	EDE-Q	HADS-A	HADS-D	LSAS	TAS-20	SRS-2	ADOS-2	WSAS
AOI face	.01	-.05	.05	.01	.05	.02	-.03	-.04	.04	.02
AOI eyes	.03	.08	-.16	-.08	-.11	-.14	-.14	-.13	.01	.02
AOI mouth	.00	-.20	.03	.08	.11	.07	.13	.14	-.03	-.05
AOI nose	.02	-.04	.03	-.05	-.09	-.05	.06	-.05	.03	-.10
Time to first fixation (face)	-.10	.25	-.07	-.27	-.18	-.05	-.07	-.18	.19	-.26
Eye-to-mouth viewing ratio	.01	.16	-.08	-.09	-.13	-.09	-.14	-.14	.01	.03

HC	Age	BMI	EDE-Q	HADS-A	HADS-D	LSAS	TAS-20	SRS-2	ADOS-2	WSAS
AOI face	.17	.30	.19	.11	-.11	-.01	-.12	-.24	-.26	.00
AOI eyes	-.06	-.10	.10	-.16	-.18	-.22	.00	-.28	-.07	.11
AOI mouth	.15	.11	-.08	.26	.14	.19	-.01	.15	.07	.12
AOI nose	-.04	-.02	-.08	-.03	-.18	-.15	-.15	-.16	-.16	-.15
Time to first fixation (face)	-.06	-.03	-.08	-.12	-.05	.01	-.14	-.15	**.42**	-.11
Eye-to-mouth viewing ratio	-.14	-.08	.15	-.19	-.19	.17	.01	-.22	-.08	-.15

ADOS-2, Autism Diagnostic Observation Schedule, 2nd edition (total score); AOI, area of interest; BMI, body mass index; EDE-Q, eating disorder examination questionnaire; HADS-A, hospital anxiety and depression scale, anxiety subscale; HADS-D, hospital anxiety and depression scale, depression subscale; LSAS, Liebowitz social anxiety scale; SRS-2, social responsiveness scale, 2nd edition; TAS-20, twenty-item Toronto alexithymia scale

Significant correlations are in bold.

Table 3. Hierarchical regression analysis predicting time spent looking at faces from associated psychopathology scores

	Model 1	Model 2	Model 3
Group			
AN vs HC	-.27*	-.19	-.14
REC vs HC	-.04	.01	.07
TAS-20		-.12	.06
SRS-2			-.28*
R^2	.06	.07	.10

AN, anorexia nervosa; HC, healthy control; REC, recovered anorexia nervosa; SRS-2, social responsiveness scale, 2nd edition; TAS-20, twenty-item Toronto alexithymia scale

Figures shown are standardized coefficients. Group was represented as two dummy variables.

* p <.05

To further explore a possible mediational effect of SRS-2 scores, a mediation analysis was run with group as the independent variable (using indicator cording, with HCs as the reference group), SRS-2 scores as the mediator, and time spent looking at faces as the dependent variable. Bias-corrected bootstrapped CIs for the indirect effects were entirely below zero (b_1 = -.03 [-.05 -.01], b_2 = -.02 [-.04 -.01]), indicating there was a significant mediation effect of group on time spent looking at faces through SRS-2 scores. The direct effect of group was not significant (c_1 = -.02, c_2 = .02, p = .117), indicating that group did not influence time spent looking at faces independent of its effect on SRS-2 scores. Thus, there was evidence of full mediation.

A hierarchical regression was run to investigate whether anxiety, depression, and ADOS-2 scores predicted time to first fixation on the face, over and above the effects of group membership. Despite the significant correlation between WSAS scores and time to first fixation in individuals with AN, this variable was not entered in the

regression due to the assumed direction of causality. Results of each regression model are presented in table 4. The full model was not significant, R^2 = .04, F(5, 123) = 1.06, p = .384, adjusted R^2 = .00. None of the included variables explained significant variance in time to first fixation on the face.

Table 4. Hierarchical regression analysis predicting time to first fixation on the face from associated psychopathology scores

	Model 1	Model 2	Model 3	Model 4
Group				
AN vs HC	-.05	-.02	-.09	-.10
REC vs HC	-.07	-.05	-.06	-.07
HADS-A		-.04	-.15	-.17
HADS-D			.20	-.17
ADOS-2				.16
R^2	.00	.00	.02	.04

ADOS-2, Autism Diagnostic Observation Schedule, 2nd edition (total score); AN, anorexia nervosa; HADS-A, Hospital Anxiety and Depression Scale, anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale, depression subscale; HC, healthy control; REC, recovered anorexia nervosa

Figures shown are standardized coefficients. Group was represented as two dummy variables.

* p <.05

5.3.5 Medication status and social attention

Independent samples t-tests comparing AN and REC participants who were taking any type of psychiatric medication (n = 37) to those who were not (n = 54) indicated no significant differences in time spent looking at faces (t(44.47) = 1.24, p = .283), time to first fixation (t(89) = -1.48, p = .142), or eye-to-mouth viewing ratio (t(89) = 0.37, p = .714). A mixed ANOVA with AOI as the within-subjects factor (eyes, nose, mouth) and medication status as the between-subjects factor showed that only the

main effect of AOI was significant, $F(1.43, 127.33) = 10.77$, $p < .001$, $\eta p^2 = .11$, confirming that participants looked at the eyes more than the nose ($p < .001$) and mouth ($p = .008$). The interaction effect ($F(1.43, 127.33) = 0.43$, $p = .583$, $\eta p^2 = .01$) and the main effect of medication status were not significant ($F(1, 89) = 0.49$, $p = .486$, $\eta p^2 = .01$).

5.4 Discussion

The current study aimed to examine attention to faces and core facial features in individuals with AN, REC, and HCs, using dynamic social stimuli. Given the high levels of comorbid psychopathology that often accompany AN, a second aim was to explore associations between comorbid traits and social attention. The main finding to emerge from the study was that participants with AN spent significantly less time looking at faces compared to REC and HCs. The association between group and time spent looking at faces was found to be fully mediated by self-reported ASD traits (SRS-2 scores). Contrary to our hypothesis, groups did not differ in their patterns of attention to individual facial features, although individuals with AN spent less time looking at facial features overall compared to REC and HCs. Further, no group differences were found in delay to first fixation to the face. Each of these findings will be discussed in turn.

Replicating previous studies using static stimuli, our results suggest reduced attention to faces in the acute state of AN (Watson et al., 2010). Given the lack of group differences in delay to first fixation on the face, this finding suggests that individuals with AN may show initial interest in orienting to social stimuli, but disengage from such stimuli more quickly than HCs. A similar pattern of results was reported by Ketelaars et al. (2017) in women with ASD. Regarding attention to the core facial features, our results differ from those reported by Harrison et al. (2019), who found reduced attention to the eyes in both acute and recovered AN compared to HCs. However, using static face stimuli, Dinkler et al. (2019) found that those recovered from AN showed no differences in attention to eyes or mouths compared to HCs, similar to the results of the current study. Again, our results in acute AN are similar to those of Ketelaars et al., who found that women with ASD fixated all parts of the

face less than HCs. These results are in contrast to a wide literature documenting reduced attention to eyes specifically in individuals with ASD (Tanaka & Sung, 2016). Ketelaars and colleagues suggest their findings might be due to differences in the male and female phenotype of ASD, with females showing enhanced social motivation and better social communication than males with ASD (Harrop et al., 2018).

Results of our mediation analysis suggested that reduced attention to faces in AN appears to be a result of the high levels of ASD traits present in this group. Although the mediation effect found provides some explanation as to why social attention may be altered in individuals with AN, the underlying mechanism is not yet known. Similar to those with ASD, it might be that attending to social stimuli results in hyperarousal, and the subsequent reduction in attention to the face represents an attempt to reduce arousal (Dalton et al., 2005). Indeed, behavioural evidence suggests higher sensitivity to social exclusion, as well as higher levels of social anxiety in AN (Cardi, Tchanturia, et al., 2018; Kerr-Gaffney et al., 2018; Meneguzzo et al., 2020). Thus, attending to social stimuli or engaging in social interactions may be uncomfortable for some individuals with AN, resulting in avoidance and reduced overall looking times.

Another explanation is that reduced attention to faces in AN may be a result of reduced social motivation, a mechanism theorised to underly social deficits in ASD (Chevallier et al., 2012). Social motivation encompasses several psychological dispositions that bias humans to attend to social stimuli, seek and take pleasure from social interaction, and foster social bonds. Indeed, there is evidence to suggest these processes are altered in AN. Along with reduced attention to faces, Watson et al. (2010) showed that in a monetary choice task, individuals with AN did not sacrifice money to see faces as HCs did, suggesting possible alterations in the reward circuitry in AN. Further, individuals with AN show high levels of social anhedonia, with studies reporting scores similar to those reported in individuals with schizophrenia (Harrison et al., 2014; Tchanturia, Davies, Harrison, et al., 2012). Further research exploring the mechanism behind reduced social attention in AN may be helpful in understanding the nature of AN and ASD comorbidity.

It is important to note that the mediation effect was only found for self-reported ASD traits, as measured by the SRS-2. In contrast, ADOS-2 scores, an observational measure of ASD traits, were not related to time spent looking at faces. There are a number of explanations for this discrepancy. Firstly, although both are measures of ASD traits, the extent to which each measure covers various traits associated with ASD likely differs. For example, difficulties with use of language are assessed in the ADOS-2, whereas the SRS-2 places relatively little emphasis on such difficulties. Four of the five subscales of the SRS-2 measure various aspects of social functioning, therefore it is perhaps not surprising that social attention is more strongly related to what is arguably a more social-oriented scale. Similarly, despite significant correlations between scores on the ADOS-2 and the SRS-2 in our population (Kerr-Gaffney et al., 2020), the two instruments likely measure slightly different constructs due to differences in self-report versus interview methods of measurement. Items in the SRS-2 assess the respondent's perceptions of their behaviour and cognitions, while the ADOS-2 directly measures behaviours during the course of the 40-50 minute interview. It could therefore be argued that the SRS-2 provides a better picture of an individual's self-perceived difficulties in everyday life. However, concerns have been raised over whether individuals with ASD are able to reflect and report on their internal beliefs and feelings in a similar way to those without ASD (Lombardo et al., 2007). Somewhat paradoxically, individuals who are higher functioning and have higher levels of social awareness may report more severe difficulties than those who are not as socially competent, as they have better insight into their difficulties than those with poorer social understanding (Bishop & Seltzer, 2012). Although our investigation has shown the SRS-2 to be a promising measure of ASD traits in individuals with AN, research examining scores on the SRS-2 in those with AN and a clinician-confirmed diagnosis of ASD are required.

A longer delay in orienting to the face was associated with higher levels of anxiety and depression (HADS scores) and functional impairment (WSAS scores) in the AN group only, and ASOS-2 scores in HCs. Studies using eye-tracking in patients with major depressive disorder demonstrate increased looking times to sad faces and other negative information, compared to HCs (Keller et al., 2019). Further, there is

some evidence to suggest reduced latency to first fixation on sad faces, a tendency which was associated with more severe depressive symptoms, in contrast to the association found in the current study (Duque & Vázquez, 2015). Given the video clip in our study was not chosen for its emotional content (though actors displayed neutral or positive expressions), comparisons with the depression literature are difficult. However, paired with the lack of association in our REC and HC groups, the results suggest a unique relationship between depressive symptoms and social attention in AN. In relation to anxiety, attentional theories propose that anxiety is associated with reduced time to fixation on threat-relevant stimuli (indicating vigilance), differently to the direction of the relationship found in the current study (Weierich et al., 2008). In our regression analysis however, neither depression, anxiety, or ADOS-2 scores explained a significant amount of variance in time to first fixation. It could be that some other unmeasured factor related to high levels of general psychopathology is responsible for the delay in fixation to faces.

Our findings have important clinical implications for understanding and treating individuals with AN. A wide literature has documented difficulties in various domains of social and emotional functioning in AN, including emotion recognition (Caglar-Nazali et al., 2014), theory of mind (Leppanen et al., 2018), empathy (Morris et al., 2014), and emotion regulation (Oldershaw et al., 2015). Despite this, social attention in AN has received very little consideration. Our findings, along with those of a recent study (Harrison et al., 2019) show that individuals with AN pay less attention to faces and core facial features when viewing dynamic, naturalistic stimuli, compared to HCs and REC. This may contribute to difficulties in social cognition, for example, in recognising emotions in others, as important nonverbal cues may be missed. In turn, these differences are likely to make social interactions and relating to others more difficult. In accordance with this hypothesis, greater work and social adjustment difficulties were significantly associated with a longer delay in attending to faces in the AN group only. Although difficulties in this domain were not associated with decreased overall looking times to faces and core features, this could be due to the measure used. The WSAS does not solely measure social functioning (it also assesses functioning in the home and private leisure activities) therefore our study may have

benefitted from using a different measure, such as the Social Functioning Questionnaire (Tyrer et al., 2005) or the Friendship Questionnaire (Baron-Cohen & Wheelwright, 2003), to further clarify relationships between social attention and self-reported social functioning.

Importantly, our results also suggest that differences in social attention in individuals with AN are due to ASD traits, rather than the eating disorder itself. Up to 50% of individuals with AN show high levels of ASD traits (Westwood et al., 2018), therefore adaptations to conventional treatments for AN might be required in this group. For example, qualitative research has shown that individuals with AN and ASD report difficulties in communicating with one another and a lack of understanding of each other's perspective, difficulties that are likely to interfere with the therapeutic relationship (Kinnaird et al., 2017, 2019). Providing psychoeducation to both patients and clinicians about different communicative styles and preferences may be helpful. Further, treatment modules designed to improve aspects of social cognition may be helpful for those with AN and high ASD traits. For example, social skills training groups have been shown to improve social cognition, friendship quality, and social skills knowledge in those with ASD (Hillier et al., 2007; Kandalaft et al., 2013; Laugeson et al., 2009; Schohl et al., 2014; Turner-Brown et al., 2008). Such interventions also report improvements in mental health outcomes, suggesting an association between social functioning and wider mental health (Hillier et al., 2011; Yoo et al., 2014). Whether such interventions might be useful for those with AN is a question for future research.

Although we cannot confirm whether participants in our study met full diagnostic criteria for ASD, the results have implications for our understanding of autism, particularly the female phenotype. Based on similarities in cognitive (e.g., set-shifting difficulties, weak central coherence, superior attention to detail, and theory of mind deficits) and behavioural profiles (e.g., perfectionism, rigid attitudes and behaviours, and narrow interests) some have argued that AN is a female manifestation of ASD (Gillberg & Råstam, 1992). Indeed, in females with ASD, who are on average diagnosed later in life than males (Lai et al., 2015), a diagnosis often comes after many years of mental health service engagement for other conditions, including anxiety,

depression, and AN (Lai et al., 2011; Mandy & Tchanturia, 2015; Vagni et al., 2016). Several barriers to detection of ASD in females have been proposed. For example, diagnostic tools have been impacted by the longstanding gender bias towards male presentations, resulting in a lack of sensitivity to female presentations (Lai et al., 2015). On average, females with ASD are less likely to display repetitive behaviours and show better surface level social skills than males with ASD (Frazier et al., 2014; Lai et al., 2011). Our findings suggest that reductions in social attention may be a transdiagnostic endophenotype, which may be helpful in understanding social cognitive processes outwith traditional diagnostic classification systems.

The current study has several limitations. Firstly, although our stimulus closely depicted what would typically be seen when interacting with others, the absence of real life interlocutor may have influenced eye movement patterns. A problem for much social attention research is that the tasks used are not inherently social – typically pictures or videos are presented on a computer screen. It may be that social attention differs in contexts where a real social interaction is expected, and this may be especially true in individuals with high levels of social anxiety, as in our study. Secondly, our study would benefit from including a subgroup of participants with AN and a diagnosis of ASD to further clarify our results. Although participants in the AN and REC groups showed relatively high levels of ASD symptoms, as evidenced by scores on both the ADOS-2 and the SRS-2, neither measure alone or in combination constitutes a diagnosis of ASD. An assessment of an individual's developmental history is also required (National Institute for Health and Care Excellence [NICE], 2012). Relatedly, although our regression analysis showed that SRS-2 scores explained a significant amount of variance in time spent looking at faces, the final model only explained a relatively small amount of variance overall, suggesting other important factors influence social attention in our sample. While age, BMI, and psychiatric medication status were not found to be associated with social attention, it is possible that other demographic or clinical factors may influence attentional processes.

To conclude, our findings demonstrate the importance of comorbid psychopathology, and specifically self-reported ASD traits in social attention in

individuals with AN. Past research has suggested considerable heterogeneity in social- and neuro-cognitive functioning in individuals with AN, possibly indicating differences in aetiological or maintenance factors (Renwick et al., 2015). Our results suggest that reduced social attention in AN may be a result of high ASD traits, in accordance with recent research demonstrating differences in set-shifting and theory of mind abilities in individuals with AN with and without high ASD traits (Anckarsäter et al., 2012; Westwood, Mandy, & Tchanturia, 2017). In order to clarify the mixed findings in related domains, future work examining social cognition in individuals with AN may benefit from including a measure of ASD traits, or indeed a subgroup of individuals with AN and a confirmed diagnosis of ASD.

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Chapter 6 - Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits

Kerr-Gaffney, J. E., Mason, L., Jones, E., Hayward, H., Ahmad, J., Harrison, A., Loth, E., Murphy, D., & Tchanturia, K. (2020). Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits. *Journal of Clinical Medicine, 9*(4), Article 1057. https://doi.org/10.3390/jcm9041057

Journal of
Clinical Medicine

MDPI

Article

Emotion Recognition Abilities in Adults with Anorexia Nervosa are Associated with Autistic Traits

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Received: 20 February 2020; Accepted: 3 April 2020; Published: 8 April 2020

Abstract: Difficulties in socio-emotional functioning are proposed to contribute to the development and maintenance of anorexia nervosa (AN). This study aimed to examine emotion recognition abilities in individuals in the acute and recovered stages of AN compared to healthy controls (HCs). A second aim was to examine whether attention to faces and comorbid psychopathology predicted emotion recognition abilities. The films expressions task was administered to 148 participants (46 AN, 51 recovered AN, 51 HC) to assess emotion recognition, during which attention to faces was recorded using eye-tracking. Comorbid psychopathology was assessed using self-report questionnaires and the Autism Diagnostic Observation Schedule–2nd edition (ADOS-2). No significant differences in emotion recognition abilities or attention to faces were found between groups. However, individuals with a lifetime history of AN who scored above the clinical cut-off on the ADOS-2 displayed poorer emotion recognition performance than those scoring below cut-off and HCs. ADOS-2 scores significantly predicted emotion recognition abilities while controlling for group membership and intelligence. Difficulties in emotion recognition appear to be associated with high autism spectrum disorder (ASD) traits, rather than a feature of AN. Whether individuals with AN and high ASD traits may require different treatment strategies or adaptations is a question for future research.

Keywords: anorexia nervosa; ASD; comorbidity; emotion recognition; attention

1. Introduction

Anorexia nervosa (AN) is a severe psychiatric disorder characterised by an intense fear of weight gain, persistent behaviour to restrict energy intake, and a disturbance in the way one's body weight or shape are experienced [1]. Difficulties in social functioning have been identified as key factors in the development and maintenance of AN [2]. For example, before illness onset, individuals with AN report more social difficulties, fewer childhood friends, and engage in more solitary activities than healthy controls (HCs) [3–6]. During the illness, a variety of difficulties are seen, including high social anxiety, poorer social skills and social problem-solving abilities, loss of interest in social activities, and reduced social networks [7–14]. Given that interpersonal difficulties are associated with poorer outcomes in those with AN [15–17], it is important to understand potential underlying socio-cognitive mechanisms.

One area that has received considerable attention is emotion recognition. Given that up to two-thirds of human communication occurs through non-verbal means, recognising emotions from faces is considered key to successful social interaction [18]. Findings from studies in individuals with AN are mixed, with some reporting those with AN are significantly less accurate at inferring emotions from faces than HCs [19–22], and others reporting no differences [23–26]. A meta-analysis of 10 studies found that individuals with AN were significantly poorer at recognising basic and complex emotions relative to HCs, with small-to-medium and large effect sizes, respectively [27]. Given the effects of starvation on higher level cognitive processes, it is important to establish whether these effects may be a result of the ill state in AN. However, very few studies have examined emotion recognition performance in those recovered from AN, and results are equally mixed. While some report performance similar to that of HCs [28], others have reported poorer emotion recognition abilities, similar to those who are acutely unwell [20,29]. It is therefore not known whether potential differences in emotion recognition abilities are a result of the ill state in AN. However, one study found that emotion recognition difficulties were also present in unaffected twins of those with AN, suggesting that difficulties in this domain might represent an endophenotype for the disorder [30].

Clinical presentation of AN is associated with high levels of depression [31], anxiety [32], alexithymia [7], and autism spectrum disorder (ASD) traits [33], factors which by themselves may alter social-cognitive abilities. It is therefore possible that comorbid psychopathology might moderate emotion recognition abilities in those with AN. Although few studies have directly investigated this issue, a few have examined the impact of alexithymia. Alexithymia is a sub-clinical trait also present within the general population, describing an inability to recognise or describe one's own emotions. When matched for levels of alexithymia, individuals with AN or bulimia nervosa (BN) have been found to show similar emotion recognition abilities to HCs [34,35], suggesting that emotion recognition difficulties may be attributable to alexithymia rather than the eating disorder (ED) per se. However, the use of mixed ED groups and small sample sizes limit interpretation of the results for AN specifically. Given the profound effects of ASD on social cognitive abilities, it is perhaps surprising that very few studies have examined the impact of ASD traits on emotion recognition in individuals with AN. Dinkler and colleagues [28] reported that individuals recovered from AN with comorbid ASD were more accurate at recognising low intensity emotional expressions than those without ASD, who did not differ from HCs. However, due to the very small sample size in the AN+ASD group ($n = 6$), analyses were treated as exploratory only. Nonetheless, these findings support the proposition that AN with or without comorbid ASD may be two qualitatively different forms of the illness [36].

Another variable that has received little attention in emotion recognition research in AN is social attention. Attending to nonverbal social cues provided by others, such as eye gaze, gestures, and facial expressions, is a necessary precursor to higher-order social cognitive abilities such as emotion recognition [37]. In typical human development, social information in the environment is highly salient, and stimuli such as faces and eyes hold particular importance [38]. This attentional bias towards social information is demonstrated from infancy, and reductions in this capacity are among one of the first signs of socio-communicative disorders such as ASD [39]. There is also emerging evidence to suggest that individuals with AN show reduced attention to faces [40] and eyes [41]. Reduced attention to facial features has been found to predict the degree of emotion recognition impairment and lower social competence in individuals with ASD [37,42,43], however only a few studies have measured attention during emotion recognition in individuals with AN. Phillipou and colleagues [44] demonstrated that while individuals with AN and HCs did not differ in their ability to recognise basic emotions, AN displayed more fixations of shorter duration to faces, indicating a "hyperscanning" strategy. Unfortunately, this study did not examine whether eye movements were associated with emotion recognition performance. In a mixed ED sample (AN or BN), Fujiwara and colleagues [35] found that difficulties in emotion recognition were predicted by less visual attention to faces in those with an ED, but not in HCs. This raises the possibility that difficulties in emotion recognition sometimes associated with EDs are a result of differences in spontaneous social attention,

rather than misinterpretation of emotional displays. Finally, Dinkler et al. [28] found no differences in eye movements between those recovered from AN and HCs, and accuracy was not associated with attention to facial features. Together, these findings suggest there may be differences in the relationship between emotion recognition and attention in the acute stage of AN compared to the recovered stage or those who have never had an ED. However, studies including an acute AN group (rather than AN and BN together) are required to test this hypothesis.

The current study aimed to examine emotion recognition performance in adults in the acute and recovered stages of AN compared to HCs. It has been suggested that difficulties in this area in those with AN may be more subtle and less detectable using basic emotions [27], therefore a paradigm allowing for assessment of both basic and complex emotion recognition was selected. In order to understand why individuals with AN might display emotion recognition deficits, a secondary aim was to examine whether visual attention to faces predicted emotion recognition performance. Relatedly, a third aim was to examine whether levels of comorbid psychopathology were associated with emotion recognition performance. As well as including measures of alexithymia and ASD traits, we included depression, anxiety, and social anxiety due to their high co-occurrence with AN [8,32,45] and potential effects on social cognition [46–51]. We hypothesised that individuals with AN would be less accurate at recognising complex emotions compared to HCs, and that those recovered from AN would show intermediate levels of performance. No significant differences in basic emotion recognition were predicted. Finally, we predicted that more attention to faces, as well as lower alexithymia and ASD traits would be associated with better emotion recognition performance.

2. Methods

Ethical approval was obtained from the National Health Service (NHS) Research Ethics Committee (Camberwell St Giles, 17/LO/1960).

2.1. Participants

All participants were required to be between 18 and 55 years old and fluent in English. Exclusion criteria were a history of brain trauma or learning disability. HC participants were recruited through a King's College London email circular and posters around campuses. Before taking part, HC participants were screened using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV) [52], to ensure they did not meet criteria for any psychiatric disorders. HCs were required to have a body mass index (BMI) between 19 and 27.

In addition to the university advertisements, participants with a lifetime history of AN were recruited through online advertisements (B-eat, call for participants, MQ Mental Health), and through two specialist NHS ED services in London. Participants were screened using the SCID-5-RV to confirm a current or past diagnosis of AN. Participants with AN were required to have a BMI $\leq$ 18.5 and recovered participants needed to have a BMI between 19 and 27.

2.2. Materials

The Films Expressions Task (FET) [53] is a facial emotion recognition task, modified to enable concurrent recording of eye movements. In each trial, participants are first presented with an emotion word on-screen. Three images are then presented for 500 ms each, one after another (with a 500 ms blank screen between images; see Figure 1). The height of each image was 15.7° at a viewing distance of 60 cm from the screen. The widths of each image were adjusted to ensure a correct aspect ratio and ranged from 12.4° to 21.4°. Images within each trial present the same actor displaying different emotional expressions (see Figure 2 for an example). Participants were then asked to indicate, as quickly and as accurately as they could, which of the images displayed the emotion word by pressing the corresponding key (1, 2, or 3). There were 53 trials in total (preceded by 3 practice trials). Prior to the task, participants were presented with a sheet listing the target emotion words and their definitions to ensure they were familiar with the words. A full list of the target emotion words is presented in the

Supplementary Materials. Images were from films made in non-English speaking countries to reduce the probability that participants would recognise the actors.

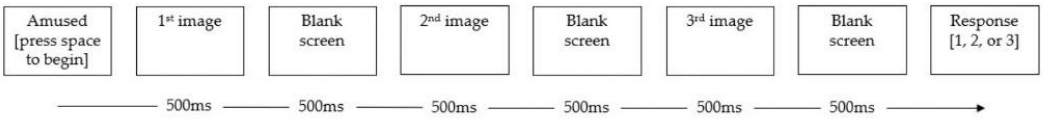

Figure 1. Sequence of events for an example trial of the films expression task.

Figure 2. Images from an example trial [amused] of the films expression task.

The FET was chosen due to its depiction of naturalistic facial expressions; its inclusion of a range of both basic and complex emotions; and relatively brief presentation times. Basic and complex emotion trials were presented interleaved in a fixed random order. Foil emotional expressions were selected to be similar to the target emotion in terms of intensity of the expression and perceptual features. Development and validation of the test stimuli is presented in [53]. Dependent measures were: Accuracy (% of trials correct), mean RTs, and time spent looking at the stimuli (as a proportion of presentation time).

The Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II) [54] measures verbal intelligence and perceptual reasoning, as well as full-scale IQ. The two subtest version was used (vocabulary and matrix reasoning).

The Autism Diagnostic Observation Schedule–2nd edition (ADOS-2), Module 4 [55] is a standardised semi-structured interview recommended for the assessment of ASD [56]. It includes a range of questions and activities designed to evoke behaviours and cognitions associated with ASD. Interviews were administered by the first author who received ADOS-2 training and met requirements for research reliability for module 4 and also attended reliability meetings throughout the study period. The revised algorithm, which was designed to more closely reflect the DSM-5 criteria for ASD was used for scoring [57]. The algorithm has two subscales: social affect and restrictive and repetitive behaviours, and total scores of 8 or more indicate possible ASD. The ADOS-2 was used in this study to identify participants with low or high ASD traits.

2.3. *Questionnaires*

The Eating Disorder Examination Questionnaire (EDE-Q) [58] measures severity of ED psychopathology. Global scores are calculated by averaging responses across items, with higher scores indicating more severe symptoms (max 6). HCs with a score of >2.7 were excluded from analyses to ensure those with possible sub-threshold ED symptoms were not included [59]. Cronbach's alpha was 0.93.

The Hospital Anxiety and Depression Scale (HADS) [60] is a 14-item scale with two subscales: anxiety and depression. Subscale scores are interpreted as: normal (0–7), mild (8–10), moderate (11–14), and severe (15–21). Cronbach's alpha was 0.93.

The Liebowitz Social Anxiety Scale (LSAS) [61] has two subscales: fear and avoidance of social situations. A score of 60 has been established as a cut-off indicative of social anxiety disorder (SAD) [62]. Cronbach's alpha was 0.97.

The Social Responsiveness Scale-2nd Edition, adult self-report form (SRS-2) [63] measures symptoms associated with ASD, with higher scores (max 195) indicating more autistic symptoms. There are 5 sub-scales: social awareness, social cognition, social communication, social motivation, and restricted and repetitive interests. Cronbach's alpha was 0.96.

The twenty-item Toronto Alexithymia Scale (TAS-20) [64] has three subscales: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. Total scores range from 0 to 100, and cut-offs are as follows: ≤51 = no alexithymia; 52–60 = borderline alexithymia; and ≥61 = alexithymia [65]. Cronbach's alpha was 0.90.

2.4. Procedure

Participants attended a testing session at the Institute of Psychiatry, Psychology & Neuroscience. After written informed consent was obtained, participants completed the FET while their eye movements were recorded using a Tobii TX300 eye-tracker. The desktop mounted eye-tracker has a sampling rate of 300 Hz, a screen resolution of 1920 × 1080, and a diagonal screen size of 23". During tracking, infrared diodes generate reflections on the participant's retinas and corneas. From this reflection the angular rotation of each eye is estimated. A five-point calibration procedure relates this angular rotation to corresponding x and y coordinates on the screen surface. Participants were seated approximately 60 cm from the screen. Stimulus presentation, behavioural data, and eye-tracking data were managed and recorded using custom-written MATLAB software [66].

After the FET, the first author administered the WASI-II and the ADOS-2, and the participant completed the questionnaires. Weight and height measurements were taken to calculate BMI (weight/height^2). Participants were reimbursed £20 for their time.

2.5. Analysis

Histograms and Q-Q plots were inspected to check for normal distributions. Where variables were positively skewed, as was the case for RT and age data, a logarithmic transformation was applied. Homogeneity was assessed using Levene's test. Group differences in psychopathology and demographic information were assessed using one-way ANOVAs and Tukey's post-hoc tests, or Welch's ANOVA with Games-Howell post-hoc tests where the assumption of homogeneity was violated.

Group differences in FET accuracy and RT were assessed with two-way mixed ANOVAs, with the within-subjects factor emotion complexity (basic or complex) and the between-subjects factor group (AN, recovered AN (REC), HC). Although analyses were conducted on log-transformed RT values, medians and interquartile range for the untransformed variable are reported for ease of interpretation, as these are similar to the geometric means. Proportion of time spent looking at faces violated the assumptions of an ANOVA (non-normal distribution, strongly negatively skewed). Therefore, group differences were assessed using the nonparametric Kruskall-Wallis test, and the effects of emotion complexity were analysed using Wilcoxon signed rank tests, with the significance level adjusted for multiple comparisons (p <0.01). Effects of medication on FET outcome measures were examined using independent samples t-tests (or a Mann-Whitney U test in the case of the non-normally distributed time spent looking at faces), comparing those with past or current AN who were on medication to those who were not.

Spearman's correlations were run to examine relationships between emotion recognition performance (the primary outcome measure), demographic variables (age, IQ, BMI), psychopathology scores (EDE-Q, HADS anxiety and depression, LSAS, SRS-2, and TAS-20, ADOS-2 total), and proportion of time spent looking at faces. Variables that showed statistically significant relationships with emotion recognition performance were entered into a hierarchical regression analysis to determine which, if any, explained variance in the outcome measure.

3. Results

3.1. Demographics

In total, 148 participants were recruited (46 AN, 51 REC, 51 HC). Five HCs were subsequently excluded based on their EDE-Q scores and one REC participant was excluded due to a BMI > 27. Due to equipment failure on the day of testing, one AN and one REC participant could not complete the FET and were therefore excluded. Thus, data from 45 participants with AN, 49 REC, and 46 HC were analysed. Eye-tracking data from three HC and one REC participant was of low quality (excessive eye blinks) and was therefore excluded from analyses, however all other data (including FET accuracy and RT) from these participants was retained.

Demographic information and psychopathology scores are presented in Table 1. There were no significant group differences in age, IQ, years of education, or sex.

Table 1. Mean (SD) demographic information and psychopathology scores.

	AN (n = 45)	REC (n = 49)	HC (n = 46)	Test Statistics	p-Value	$\eta p^2/d$
Age (years) †	27.04 (8.92)	26.00 (8.10)	23.87 (4.52)	F (2, 85.23) = 2.16	0.12	0.02
% female	93.5	98.0	91.1	Fisher's exact test = 2.17	0.31	
BMI	15.75 (1.41) ^{a}	21.14 (1.91) ^{b}	21.69 (1.88) ^{b}	F (2, 136) = 159.75	**<0.001**	0.70
Years of education	16.06 (3.07)	16.52 (2.62)	16.63 (2.45)	F (2, 136) = 0.54	0.58	0.01
IQ	110.86 (12.29)	110.16 (10.38)	113.78 (7.25)	F (2, 85.30) = 2.18	0.12	0.02
Age diagnosed †	19.84 (7.39) ^{a}	16.41 (3.53) ^{b}	-	t (73.24) = 2.92	**0.01**	0.59
Illness length (years)	7.19 (7.88)	5.40 (5.65)	-	t (79.67) = 1.24	0.22	0.26
% on psychiatric medication	53.3 ^{a}	32.7 ^{b}	-	χ^2 = 4.10	**0.04**	
EDE-Q	3.86 (1.25) ^{a}	1.81 (1.52) ^{b}	0.61 (0.58) ^{c}	F (2, 75.81) = 125.35	**<0.001**	0.56
HADS-A	13.56 (4.51) ^{a}	10.84 (5.11) ^{b}	5.02 (3.09) ^{c}	F (2, 87.46) = 61.90	**<0.001**	0.40
HADS-D	9.87 (4.40) ^{a}	5.04 (4.02) ^{b}	1.54 (1.68) ^{c}	F (2, 76.50) = 77.66	**<0.001**	0.48
LSAS	68.95 (30.78) ^{a}	57.08 (29.98) ^{a}	27.91 (18.32) ^{b}	F (2, 84.80) = 36.34	**<0.001**	0.29
SRS-2	82.43 (31.99) ^{a}	70.04 (31.97) ^{a}	39.23 (20.18) ^{b}	F (2, 85.60) = 34.67	**<0.001**	0.28
TAS-20	58.16 (13.50) ^{a}	49.81 (15.08) ^{b}	37.47 (11.26) ^{c}	F (2, 136) = 26.86	**<0.001**	0.29
ADOS-2						
Total	4.67 (3.94) ^{a}	4.16 (4.50) ^{ab}	2.70 (2.52) ^{b}	F (2, 85.99) = 4.79	**0.01**	0.05
SA	4.02 (3.61) ^{a}	3.71 (3.96) ^{ab}	2.50 (2.38) ^{b}	F (2, 86.95) = 3.48	**0.04**	0.04
RRB	0.64 (1.00) ^{a}	0.45 (0.89) ^{ab}	0.20 (0.58) ^{b}	F (2, 86.10) = 3.82	**0.03**	0.05
% above clinical cut-off	17.8 ^{a,b}	24.5 ^{a}	4.3 ^{b}	χ^2 = 7.48	**0.02**	

ADOS-2: autism diagnostic observation schedule–2nd edition; AN: anorexia nervosa; BMI: body mass index; EDE-Q: eating disorder examination questionnaire; HADS-A: hospital anxiety and depression scale, anxiety subscale; HADS-D: hospital anxiety and depression scale, depression subscale; HC: healthy control; IQ: intelligence quotient; LSAS: Liebowitz social anxiety scale; REC: recovered anorexia nervosa; RRB: restrictive and repetitive behaviors; SA: social affect; SD: standard deviation; SRS-2: social responsiveness scale–2nd edition; TAS-20: twenty-item Toronto alexithymia scale. Different superscripts indicate significant differences between groups, significant p-values are highlighted in bold. † Variable was log transformed for analyses, original values are displayed.

3.2. Films Expression Task

Mean emotion recognition accuracy, RTs, and proportion of time spent looking at faces across groups are displayed in Table 2. A 3 (group: AN, REC, HC) × 2 (emotion complexity: basic, complex) mixed ANOVA was computed to examine group differences in emotion recognition accuracy (% correct) for basic and complex emotions. The interaction effect was not significant, though it did reach trend level, F (2, 137) = 2.43, p = 0.09, ηp^2 = 0.03. The main effect of emotion complexity was significant, F (1, 137) = 26.65, p <0.001, ηp^2 = 0.16, indicating accuracy was significantly higher for basic emotions (M = 89.34%, SD = 10.92%) than complex ones (M = 85.44%, SD = 10.19). The main effect of group was not significant, F (2, 132) = 1.10, p = 0.34, ηp^2 = 0.02. Accuracy (all faces) did not differ between medicated and unmedicated participants t (92) = 0.42, p = 0.67.

Table 2. Mean (SD) performance and attention during the films expression task.

	AN (n = 45)	REC (n = 49)	HC (n = 46)
Accuracy (% correct)			
Basic emotions	88.25 (11.61)	89.80 (12.88)	89.91 (7.62)
Complex emotions	84.10 (10.79)	84.09 (11.65)	88.18 (7.14)
Reaction time (ms) †			
Basic emotions	786.86 (546.32)	668.86 (415.61)	556.61 (352.43)
Complex emotions	875.69 (597.10)	703.59 (518.45)	662.13 (376.79)
Time spent looking at faces (%)			
Basic emotions	95.79 (5.85)	97.60 (2.79)	94.60 (8.23)
Complex emotions	96.54 (5.26)	97.81 (2.64)	94.37 (8.64)

AN: anorexia nervosa; HC: healthy control; REC: recovered anorexia nervosa; SD: standard deviation. † Variable was log transformed for analyses, median and IQR (of the untransformed variable) are displayed.

A 3 (group: AN, REC, HC) × 2 (emotion complexity: basic, complex) mixed ANOVA was computed to examine group differences in RTs for basic and complex emotions. The interaction effect was not significant, F (2, 132) = 0.86, p = 0.43, ηp^2 = 0.01. The main effect of emotion complexity was significant, F (1, 137) = 60.72, p <0.001, ηp^2 = 0.31, indicating RTs were significantly shorter for basic emotions (median = 654.14 ms, IQR = 464.68 ms) than complex ones (median = 718.29 ms, IQR = 474.55 ms). The main effect of group was not significant, F (2, 137) = 2.06, p = 0.13, ηp^2 = 0.03. RTs (all trials) did not differ between medicated and unmedicated participants, t (92) = −1.03, p = 0.31.

Kruskall-Wallis tests indicated there were no significant differences between groups in the proportion of time spent looking at faces displaying basic emotions, χ^2 (2) = 4.75, p = 0.09, or complex ones, χ^2 (2) = 4.61, p = 0.10. Wilcoxon signed-ranks tests indicated that time spent looking at basic versus complex emotions did not significantly differ within either of the three groups (all p >0.01, adjusted significance level for multiple comparisons). Proportion of time spent looking at faces (overall) did not differ between medicated and unmedicated participants, U = 980.00, p = 0.57.

3.3. Predicting Emotion Recognition Performance

In the whole sample, emotion recognition accuracy was significantly positively associated with the proportion of time spent looking at faces (r = 0.17, p = 0.04) and IQ (r = 0.23, p = 0.01), and negatively correlated with TAS-20 (r = −0.18, p = 0.04) and ADOS-2 scores (r = −0.17, p = 0.04) (see Supplementary Materials for full table of correlations). To establish whether the relationship between accuracy and attention to faces differed across groups, correlations were run for each of the three groups separately. Proportion of time spent looking at faces significantly correlated with emotion recognition accuracy in the AN group only (r = 0.34, p = 0.02). However, a linear regression showed that proportion of time spent looking at faces did not significantly predict emotion recognition abilities in those with AN, although the association did reach trend level, F (1, 42) = 3.36, p = 0.07, adjusted R^2 = 0.05. In the whole sample, a hierarchical multiple regression was run to determine if the addition of attention to faces, TAS-20, and ADOS-2 scores would improve the prediction of emotion recognition performance over group membership and IQ. The full model was significant, R^2 = 0.22, F (6, 126) = 5.95, p <0.001, adjusted R^2 = 0.18. Details of each regression model are shown in Table 3. The addition of ADOS-2 scores (model 3) led to a significant increase in R^2 of 0.11, F (1, 127) = 17.54, p <0.001. The addition of proportion of time spent looking at faces (model 2) and TAS-20 scores (model 4) did not significantly add to the prediction.

Table 3. Hierarchical regression analysis predicting emotion recognition accuracy from associated demographic variables and psychopathology scores.

	Model 1	Model 2	Model 3	Model 4
IQ	0.22 *	0.23 **	0.17 *	0.15
% of time spent looking at faces		0.17	0.10	0.11
ADOS-2			−0.35 ***	−0.31 ***
TAS-20				−0.14
R^2	0.07	0.10	0.21	0.22

ADOS-2: autism diagnostic observation schedule–2nd edition; IQ: intelligence quotient; TAS-20: twenty-item Toronto Alexithymia Scale. Figures shown are standardized coefficients. Group membership was entered in model 1 but was not significant and not displayed here. * p <0.05; ** p <0.01; *** p <0.001.

3.4. ASD, Emotion Recognition Performance, and Attention to Faces

To further explore the relationship between ASD symptoms and emotion recognition performance, individuals with past or current AN were grouped according to whether they met the clinical cut-off for ASD on the ADOS-2 and compared with HCs. The two HCs who scored above cut-off on the ADOS-2 were excluded, due to their being too few cases to assess group differences. Thus, 44 HC, 20 lifetime AN scoring above the ADOS-2 cut-off (AN + ASD), and 74 lifetime AN scoring below the ADOS-2 cut-off (AN − ASD) were included in analyses.

A 3 (group: AN + ASD, AN − ASD, HC) × 2 (emotion complexity: basic, complex) mixed ANOVA was computed to examine group differences in emotion recognition accuracy (Figure 3). The interaction effect was not significant, though it did reach trend level, $F(2, 135) = 2.70$, $p = 0.07$, $\eta p^2 = 0.04$. The main effect of emotion complexity was significant, $F(1, 135) = 23.13$, p <0.001, $\eta p^2 = 0.15$, indicating accuracy was significantly higher for basic emotions (M = 89.34%, SD = 10.99%) than complex ones (M = 85.49%, SD = 10.22). The main effect of group was also significant, $F(2, 135) = 10.51$, p <0.001, $\eta p^2 = 0.14$, indicating AN + ASD (M = 77.36%, SD = 16.54%) were significantly less accurate at recognising emotions than AN − ASD (M = 87.58, SD = 7.36), and HCs (M = 88.85%, SD = 6.10%), who did not differ from one another. Kruskall-Wallis tests indicated there were no significant differences across groups in the proportion of time spent looking at faces displaying basic emotions χ^2 (2) = 2.06, $p = 0.36$, or complex ones, χ^2 (2) = 2.92, $p = 0.23$.

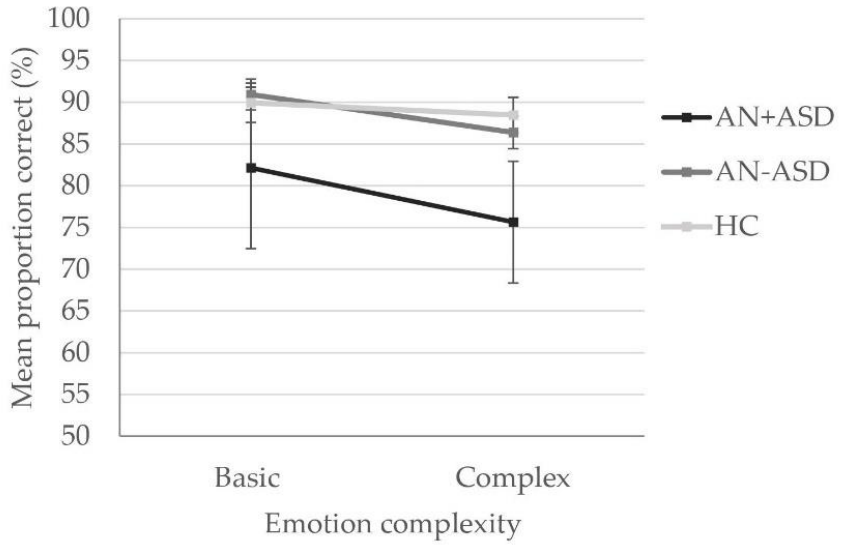

Figure 3. Mean proportion of correct trials on the films expression task. Error bars represent 95% confidence intervals. HC = healthy controls; AN + ASD = lifetime AN, above cut-off on the ADOS-2; AN − ASD = lifetime AN, below cut-off on the ADOS-2.

4. Discussion

The current study aimed to examine emotion recognition abilities in those with acute AN, REC, and HCs. Contrary to our hypotheses, there were no significant differences between groups in basic or complex emotion recognition. Our prediction that emotion recognition abilities would be associated with attention to faces, as well as alexithymia and ASD traits, was partially supported. Emotion recognition accuracy was significantly positively correlated with proportion of time spent looking at faces, and negatively correlated with alexithymia (TAS-20) and autistic features (ADOS-2 scores). However, in regression analyses, only ADOS-2 scores remained a significant predictor of emotion recognition performance while controlling for IQ and group membership. A subsequent analysis demonstrated that considering acute and recovered AN together, those who scored above the clinical cut-off for ASD on the ADOS-2 were significantly less accurate at recognising emotions than those who scored below the ADOS-2 cut off and HCs. These groups did not differ in the proportion of time spent looking at faces, suggesting differences in emotion recognition abilities were not due to differences in attention. Thus, in our sample of adults with a lifetime diagnosis of AN, difficulties in emotion recognition abilities appear to be associated with high ASD traits, rather than a feature of AN.

Our findings suggest that difficulties in emotion recognition are not a feature of the socio-emotional profile hypothesised to contribute to the maintenance of AN [2]. Although our results contrast with studies showing facial emotion recognition difficulties in acute and recovered AN [19,20,29,67], several studies have failed to detect significant differences between groups [23–25,68,69]. It is possible that the different emotion recognition tasks used across studies contribute to the mixed results. The FET was chosen for its relative difficulty; faces are presented for 500 ms only, stimuli are naturalistic facial expressions, and a wide range of complex emotions are included in addition to the six basic emotions. Nonetheless, given that accuracy was relatively high across groups, it may be the case that there were ceiling effects in our sample. This might be due to educational levels or IQ; participants were generally highly educated and mean IQ scores across groups were higher than the population average. Indeed, in the original pilot studies of the FET, distractors were only chosen if they were misidentified as the target emotion less than 30% of the time [53], possibly resulting in the high level of accuracy seen in our sample. It should be noted that the FET has not yet been validated in a normative sample, limiting comparisons with previous literature. However, a recent study using the FET found that individuals with ASD were significantly less accurate at identifying emotions and displayed longer RTs compared to HCs [70]. Mean accuracy in the HC group (87.5% correct) was very similar to that obtained in our sample (88.64%), whereas performance in the ASD group was far lower (70.8%) than in our clinical group (acute AN = 85.2%). Although definitive conclusions cannot be made from cross-study comparisons, this pattern supports intact emotion recognition performance in acute and recovered AN.

Another explanation for the mixed results from emotion recognition studies in AN concern another of our main findings: ASD traits predicted performance rather than ED status. It could be the case that variations in ASD symptoms across study samples contribute to the mixed findings, such that group differences in mean performance may not be apparent in samples with relatively low levels of ASD traits. To further investigate this issue, future studies may benefit from looking beyond group differences in social-cognitive performance. For example, Renwick and colleagues [36] used cluster analysis to explore social- and neuro-cognitive abilities in adults with AN, including measures of set-shifting, central coherence, and theory of mind (ToM). Three clusters emerged: One characterised by average to high social- and neuro-cognitive performance; another showing mixed performance (good set-shifting, average ToM, and poor central coherence and cognitive flexibility); and a final cluster characterised by poor overall performance. The authors propose that the third cluster, which comprised 17% of participants, represented an "ASD-like" cluster. Unfortunately, no diagnostic or self-report measures of ASD were included in the study, so is in not known whether these participants met diagnostic criteria for ASD. Nonetheless, this study demonstrates that distinct sub-groups within the overall diagnosis of AN may exist, potentially with different aetiologies and developmental pathways.

Although our cross-sectional design prevents conclusions regarding the differing developmental pathways that may characterise participants in the current study, recent research presents some interesting hypotheses. For example, individuals with ASD report sensory sensitivities and a limited range of acceptable foods, often from childhood [71,72]. Further, women with ASD report high levels of eating disturbances compared to both men with ASD and neurotypical women, particularly in regards to eating rituals, sensory sensitivity to the taste, smell, and texture of food, and difficulties around eating with others [73]. These difficulties may reinforce food restriction, resulting in energy deficits and a potential trigger for the development of a clinical ED in some individuals with ASD [74]. Another possible pathway through which EDs and ASD may co-occur is via interacting influences of body dissatisfaction and gender identity. There is emerging evidence to suggest that having ASD increases one's chances of experiencing gender dysphoria [75] and rejecting a binary gender identity [76]. In addition, qualitative reports from women with ASD often report conflict between expected feminine roles and their autistic identities [77]. At the same time, transgender individuals are at increased risk of body dissatisfaction and clinical EDs [78,79]. Specifically, restrictive eating and exercise can be a means of achieving a body congruent with one's gender identity [80]. These differing aetiological pathways and maintenance factors for EDs are likely to have important implications for treatment.

The findings from the current study have important clinical implications. In our sample, 17.8% of acute AN and 24.5% of REC scored above the clinical cut-off on the ADOS-2, compared to 4.3% of HCs. Similar findings have been reported previously [69,81]. Interestingly, total scores on the ADOS-2 were significantly higher in acute AN than HCs, while scores in the REC group lay between the two. This pattern of results suggests that although a small proportion of ASD symptoms may be a result of starvation in acute AN, the ADOS-2 algorithm might be robust against picking up false positives. The findings from our recovered group suggest that ASD symptoms may be a stable trait, present before and after the illness in individuals with AN. Consequently, a more personalised approach to treatment in individuals with AN might be required. Treatment modules designed to improve social cognition may not be suitable for the majority of individuals with AN, however, they could prove useful in those with high ASD traits and accompanying emotion recognition difficulties. Interventions such as social skills training groups may be effective in adults and adolescents with ASD, with several studies reporting improvements in social cognition measures, social skills knowledge, and friendship quality [82–86]. In addition, some studies have shown improvements in mental health outcomes, suggesting a relationship between social functioning and wider mental health [87,88]. Whether such interventions might be useful for those with AN and ASD comorbidity is yet to be addressed. Thus far, interventions in AN that have incorporated emotion or social skills training, such as Cognitive Remediation and Emotion Skills Training (CREST) [89] have more heavily emphasised identifying and managing one's own emotions rather than identifying emotions in others. Future treatment protocols may benefit from the inclusion of more extensive social cognition training specifically for those with AN and comorbid ASD.

The current study has a number of strengths. The sample size is one of the largest among eye-tracking studies in individuals with EDs (for a review, see [90]), and it is the first study to measure attention during emotion recognition in both acute and recovered AN. The inclusion of both basic and complex emotions, as well as the use of realistic photo stimuli allowed for a more ecologically valid assessment of emotion recognition abilities. However, several limitations should also be discussed. Most notably, given the short stimuli presentation times (500 ms), our paradigm only provided an assessment of early attentional engagement during emotion recognition. It may be that individuals with AN show differences in attention at later processing stages where attention is under conscious control [91]. This may explain why although attention to faces significantly correlated with emotion recognition accuracy, it did not explain a significant amount of the variance in accuracy in regression analyses. Although our quick presentation times might have replicated the fleeting facial expressions encountered in real life, future studies would benefit from measuring attention over longer periods in order to gain a better understanding of attentional processes in individuals with AN. Further, given the

inclusion of both basic and complex emotion words in the FET, it is likely that verbal comprehension abilities explain significant variance in accuracy. Although we assessed associations between full-scale IQ and emotion recognition accuracy, our analyses may have benefited from including verbal IQ instead. Nonetheless, our findings show that individuals with AN have the capacity to process emotions rapidly to the same extent as HCs.

Relatedly, the short stimuli presentation times in the FET prevented a more fine-grained analysis of scan paths across the facial features. Reduced attention to the eyes has been demonstrated in acute AN during free viewing of face images, as well as during real-life social interactions [40,41]. Thus, it could be the case that our measure of overall looking times to faces was too blunt to detect group differences. Another limitation of the current study is the cross-sectional design. It cannot be ruled out that differences in socio-cognitive functioning or psychological resources contributed to the recovery of the recovered AN group. To our knowledge, no study has tested emotion recognition abilities and/or social attention over time in the same group of individuals with AN before and after recovery. Further, it must be noted that although the ADOS-2 is recommended as part of an ASD diagnostic assessment, it does not provide enough information on its own to confer a diagnosis of ASD [56]. Research using developmental measures in addition to assessing current symptoms would be informative in further defining social cognition in the AN+ASD sub-group.

To conclude, the findings of the current study suggest that emotion recognition difficulties are not a feature of the socio-emotional phenotype proposed to characterise AN. Instead, difficulties in emotion recognition appear to only be present in those with high ASD traits, independent of illness state. While it is not known whether this subgroup of individuals meets full diagnostic criteria for ASD, our findings support the notion that AN with and without high ASD traits might be two qualitatively different conditions. Whether these individuals may require different treatment strategies or adaptations to accommodate different communicative styles is a question for future research. Our results also suggest individuals in the acute and recovered stages of AN do not show any differences in attention to faces compared to HCs. However, given the limitations of our study design and the lack of research in this area, future studies should examine attention to individual facial features to expand on our findings.

Supplementary Materials: The following are available online at http://www.mdpi.com/2077-0383/9/4/1057/s1, Table S1: Target emotions in the films expression task; Table S2: Correlations between FET accuracy, time spent looking at faces, and clinical and demographic variables in the full sample.

Author Contributions: Conceptualization, J.K.-G. and K.T.; formal analysis, J.K.-G. and E.J.; funding acquisition, J.K.-G.; investigation, J.K.-G.; methodology, E.L. and J.A.; resources, H.H. and D.M.; software, L.M.; supervision, A.H., D.M. and K.T.; writing—original draft, J.K.-G.; writing—review & editing, L.M., E.J., H.H., A.H., E.L., J.A. and K.T. All authors have read and agreed to the published version of the manuscript.

Funding: J.K. is supported by a doctoral studentship from the Economic and Social Research Council (ESRC) and received research funding from the Psychiatry Research Trust. A.H. is funded by the Medical Research Council (MRC) (MR/S020381/1). K.T. would like to acknowledge MRC-MRF Fund (MR/R004595/1); the Health Foundation, an independent charity committed to bring better health care for people in the UK (1115447); and the Maudsley Charity for their support. The Maudsley Charity is an independent NHS mental health charity which works in partnership with patients and families, clinical care teams and researchers at South London and Maudsley NHS Foundation Trust, the Institute of Psychiatry, Psychology and Neuroscience, King's College London, and community organisations, with a common goal of improving mental health, to support innovation, research and service improvement.

Acknowledgments: The authors would like to thank the participants who took part in the research for their time.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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6.1 Supplementary material

Supplementary table 1. Target emotions in the films expression task

Basic	Happy Angry Sad Afraid Surprised Disgusted
Complex	Accusing Affectionate Amused Confident Defiant Despairing Disappointed Disbelieving Eager Furious Hostile Hurt Intimidating Joking Mocking Pleading Pleased Resentful Satisfied Shocked Suspicious Thoughtful Uneasy

Supplementary table 2. Correlations between FET accuracy, time spent looking at faces, and clinical and demographic variables in the full sample

	FET accuracy	FET duration	Age[†]	IQ	BMI	EDE-Q	HADS-A	HADS-D	LSAS	TAS-20	SRS-2	ADOS-2
FET accuracy	-											
FET duration	**.17**	-										
Age[†]	.03	.03	-									
IQ	**.23**	-.03	.15	-								
BMI	.15	.01	-.09	.11	-							
EDE-Q	-.08	.01	.09	-.20	**-.51**	-						
HADS-A	-.15	**.21**	.03	-.22	**-.47**	**.74**	-					
HADS-D	-.16	.09	-.01	-.15	**-.55**	**.75**	**.77**	-				
LSAS	-.06	**.21**	-.11	**-.24**	**-.34**	**.67**	**.69**	**.70**	-			
TAS-20	**-.18**	.07	**-.19**	**-.23**	**-.45**	**.63**	**.67**	**.70**	**.69**	-		
SRS-2	-.15	.13	-.17	**-.29**	**-.38**	**.62**	**.70**	**.73**	**.75**	**.76**	-	
ADOS-2	**-.17**	.10	**-.17**	-.06	**-.19**	**.26**	**.23**	**.24**	**.24**	**.34**	**.28**	-

ADOS-2, autism diagnostic observation schedule, 2nd edition; BMI, body mass index; EDE-Q, eating disorder examination questionnaire; FET accuracy, proportion correct on the films expression task; FET duration, proportion of time spent looking at faces; HADS-A, hospital anxiety and depression scale, anxiety subscale; HADS-D, hospital anxiety and depression scale, depression subscale; IQ, intelligence quotient; LSAS, Liebowitz social anxiety scale; SRS-2, social responsiveness scale, 2nd edition; TAS-20, twenty-item Toronto alexithymia scale

Significant correlations are in bold.

† Variable was log transformed for analyses, original values are displayed.

Chapter 7 - Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2019). Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis. *Frontiers in Psychiatry, 10,* Article 102. https://doi.org/10.3389/fpsyt.2019.00102

frontiers in Psychiatry

SYSTEMATIC REVIEW
published: 04 March 2019
doi: 10.3389/fpsyt.2019.00102

Cognitive and Affective Empathy in Eating Disorders: A Systematic Review and Meta-Analysis

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OPEN ACCESS

Edited by:
Dessa Bergen-Cico,
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Sarah Louise Mason,
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Specialty section:
This article was submitted to
Social Cognition,
a section of the journal
Frontiers in Psychiatry

Received: 27 November 2018
Accepted: 12 February 2019
Published: 04 March 2019

Citation:
Kerr-Gaffney J, Harrison A and
Tchanturia K (2019) Cognitive and
Affective Empathy in Eating Disorders:
A Systematic Review and
Meta-Analysis.
Front. Psychiatry 10:102.
doi: 10.3389/fpsyt.2019.00102

Background: Recent models of eating disorders (EDs) have proposed social and emotional difficulties as key factors in the development and maintenance of the illness. While a number of studies have demonstrated difficulties in theory of mind and emotion recognition, little is known about empathic abilities in those with EDs. Further, few studies have examined the cognitive-affective empathy profile in EDs. The aim of this systematic review and meta-analysis was to provide a synthesis of empathy studies in EDs, and examine whether those with EDs differ from healthy controls (HC) on self-reported total, cognitive, and affective empathy.

Methods: Electronic databases were systematically searched for studies using self-report measures of empathy in ED populations. In total, 17 studies were identified, 14 of which could be included in the total empathy meta-analysis. Eight of the 14 studies were included in the cognitive and affective empathy meta-analyses.

Results: Meta-analyses showed that while total empathy and affective empathy scores did not differ between those with anorexia nervosa (AN) and HC, those with AN had significantly lower cognitive empathy scores compared to HCs (small effect size). Meta-analyses of Interpersonal Reactivity Index sub-scores revealed that AN had significantly lower Fantasy scores than HC (small effect size), indicating that those with AN have more difficulty in identifying themselves with fictional characters. Only 3 studies examined empathy in those with bulimia nervosa (BN) or binge eating disorder (BED).

Conclusions: The lowered cognitive empathy and intact affective empathy profile found in AN is similar to that found in other psychiatric and neurodevelopmental conditions, such as autism spectrum disorder (ASD). These findings add to the literature characterizing the socio-emotional phenotype in EDs. Future research should examine the influence of comorbid psychopathology on empathy in EDs.

Keywords: empathy, eating disorders, anorexia nervosa, autism, self-report, insight

INTRODUCTION

Rationale

Empathy refers to our ability to understand and identify the mental states of others, as well as our ability to share the feelings of others (1). It is considered a key component of social cognition, cooperation, and prosocial behavior, as it allows us to make sense of and respond appropriately to other people's behavior (2). Empathy can be separated into two major facets. Cognitive empathy refers to the ability to recognize and understand another's mental state (part of theory of mind (ToM) or mentalising) while affective empathy is the ability to share the feelings of others, without any direct emotional stimulation to oneself (3). As an illustrative example, sharing the excitement of a close friend's job offer is fundamentally different from understanding that your friend must be having thoughts and feelings, and what these feelings might be. These two aspects of empathy rely on different brain structures and take different developmental pathways, with affective empathy developing much earlier than cognitive empathy (1).

Differences in empathic abilities have been observed in a number of psychiatric disorders including schizophrenia (4, 5), autism spectrum disorder [ASD; (6, 7)], borderline personality disorder [BPD; (8)], and depression (9). Importantly, far from there being a universal deficit in empathic abilities, research in these psychiatric disorders shows that there is often a difficulty in a specific aspect of empathy, while other empathic abilities remain intact. For example, it has been found that those with ASD have problems with cognitive empathy, but do not differ from neurotypical controls in affective empathy (10). Reduced attention to informative social information may provide one explanation for the problems in cognitive empathy seen in those with ASD. For example, it is reported that individuals with ASD pay less attention to faces, and especially eyes (11), and this is associated with poorer emotion recognition and ToM ability (12–14), as well as lower social competence (15). Similarly, while healthy controls (HCs) show significantly higher levels of cognitive empathy compared to affective empathy, those with BPD show significantly poorer cognitive empathy than HCs, and slightly increased levels of affective empathy (16). In bipolar disorder (BD), this cognitive/affective empathy distinction is further complicated by clinical state. In both manic and depressive phases of illness, there is an impairment in cognitive empathy compared to HCs. However, during the manic phase, affective empathy is significantly higher than in HCs and patients in the depression phase of BD, who did not differ from one another (17). Increased affective empathy in BPD and BD may be related to disturbances in emotion inhibition.

Recent models of eating disorders (EDs) have put forward social and emotional difficulties as key factors in the development and maintenance of the illness (18, 19). However, relatively little is known about the specific empathy profile in those with EDs. Based on longitudinal research in a community sample from Sweden, Gillberg et al. published a number of papers reporting a subgroup of AN patients with "empathy disorders"—those that had severe problems in social understanding and communication, consistent with ASD (20). Poorer outcomes were found in this group (21, 22). Since then, a growing body of evidence has documented overlap between symptoms in ASD and AN. For example, both groups show high levels of social anxiety (23, 24) and alexithymia (25, 26), differences in social attention (11, 27, 28), and poorer emotion recognition (29, 30) and ToM ability (31, 32). Reduced social networks have been documented in AN and bulimia nervosa (BN) (33, 34), as well as difficulties in understanding the concept of friendship (35). It is possible that reduced empathic abilities, along with communication difficulties, may contribute to the diminished social networks and isolation that characterize EDs. Given that interpersonal difficulties are associated with more severe ED psychopathology (36, 37), understanding mechanisms that may contribute to these problems may be helpful in improving outcomes in those with these EDs.

Objectives

The aim of this systematic review and meta-analysis is to provide a synthesis of empathy research in EDs. Previous reviews on social processes in EDs have ascribed relatively little attention to the topic, and focus on emotion recognition rather than other aspects of empathy such as affect sharing [e.g., (31)]. In addition, new studies have been published in the intervening years. An additional aim is to examine potential differences between those with EDs and HCs in the specific types of empathy (self-reported cognitive and affective empathy), to permit better comparisons with other psychiatric populations. Self-reported empathy measures will be the focus of this review, in order to elicit patients' views and self-assessment of their skills.

Research Questions

The research questions are as follows: (1) do levels of self-reported empathy differ in those with EDs compared to HCs? (2) do levels of cognitive and affective empathy differ between EDs and HCs? (3) are empathy levels associated with any psychopathological or clinical variables?

METHODS

Systematic Review Protocol

The review and meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (38).

Eligibility Criteria

Studies using a self-report measure of empathy were included. Inclusion criteria were: (1) means and standard deviations reported for empathy scores in at least one clinical ED group and a HC group (2) the clinical ED group met criteria for any ED diagnosis, according to DSM or ICD criteria (3) full article available in English (4) published in a peer reviewed journal. Articles that examined disordered eating samples rather than a clinical ED were not included.

Data Sources and Search Strategy

The electronic databases SCOPUS, Web of Science, PsycInfo, and PubMed were searched for papers up to September 2018. The

following search terms were used: anorexia nervosa OR bulimia nervosa OR eating disorder AND empathy OR emotional empathy OR empathic concern OR interpersonal reactivity. No other search limits were applied, with the exception of Web of Science, where results were filtered by the ED term for relevance. Reference lists were also searched for relevant papers.

Study Selection

The selection process for studies is displayed in **Figure 1**. In total, the search generated 644 records. After removing duplicates, 122 records were assessed for relevance based on article titles. If titles were ambiguous or potentially relevant, records were retained and their abstracts screened against the eligibility criteria. This resulted in 61 abstracts being screened, 19 of which were excluded as they did not meet eligibility criteria. After screening of abstracts, 42 potentially eligible full-text articles were identified. One study included a sample of participants with BN, however at the time of publication, BN was not yet included in the DSM. The study was included in the review as participants had a clinical diagnosis of BN. If means and standard deviations for individual groups were not reported, study authors were contacted. If no response was received, studies were excluded. Evaluation of these full texts resulted in 25 studies being excluded, and 17 studies being included in the review.

Data Extraction

The following data was extracted from each paper that met all eligibility criteria: number of participants in each group, mean age, mean body mass index (BMI), percentage of female participants, empathy measure used, mean empathy scores, and any subscale scores, if they were reported. Where studies reported sub-scale scores only, total, cognitive, and affective empathy scores were calculated so that studies could be included in meta-analyses.

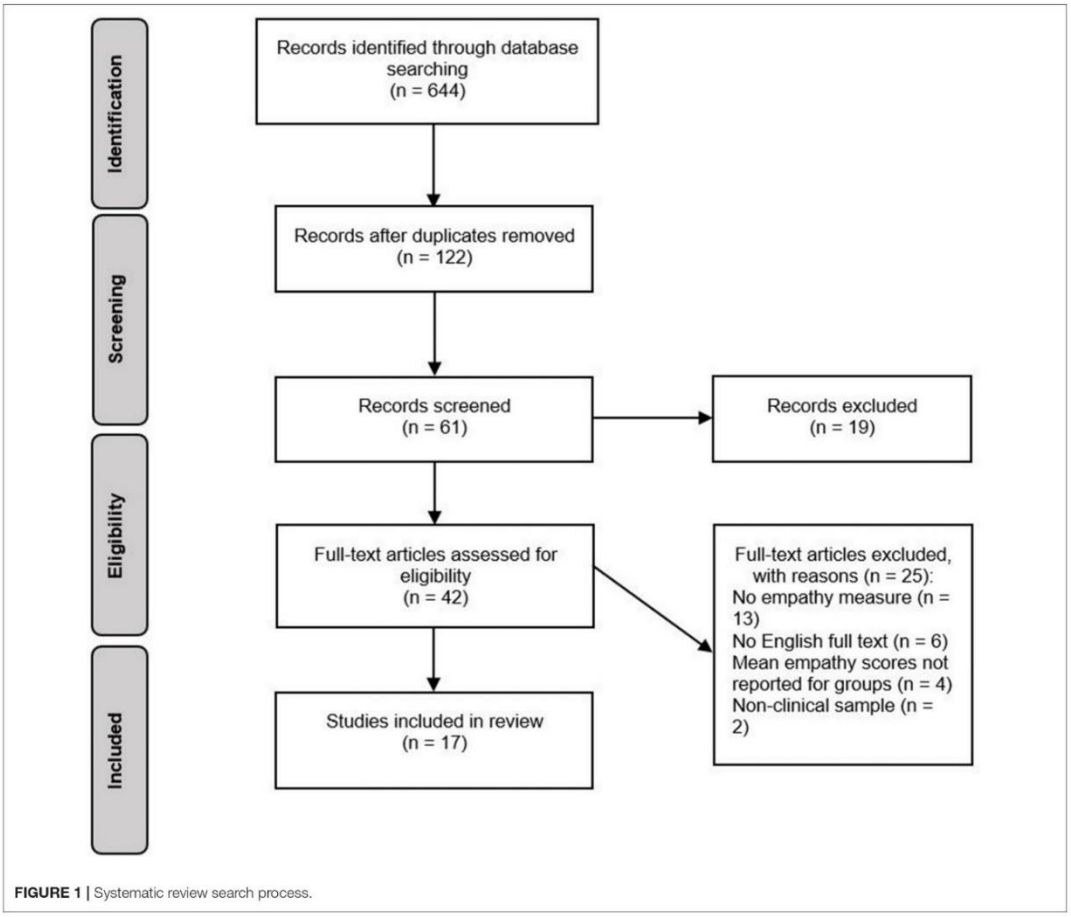

FIGURE 1 | Systematic review search process.

TABLE 1 | Characteristics of studies.

References	Group	Mean age (SD)	Mean BMI (SD)	% female	Empathy measure	Mean (SD) total empathy	Subscales reported?	
							Mean (*SD*) cognitive empathy	Mean (*SD*) affective empathy
Adenzato et al. (45)	30 AN	19.73 (6.06)	15.06 (1.74)	100	EQ	**44.17 (11.47)**	NR	NR
	32 HC	20.47 (2.72)	20.21 (1.45)	100		**50.72 (8.35)**		
Aloi et al. (46)	22 BED	43.8 (10.7)	36.9 (4.2)	81.4	EQ	41.8 (14.9)	NR	NR
	16 sub-threshold BED	42.5 (11.3)	37.5 (4.5)	68.8		50.5 (11.6)		
	20 obese controls	50.6 (8.6)	38.2 (6.5)	45		50.1 (12.4)		
Baron Cohen et al. (47)	66 AN	17.85 (0.39)	NR	100	EQ (adult and adolescent versions)†	**Younger: 44.7 (16.4)** Older: 49.6 (9.7)	NR	NR
	1609 HC	18.56 (3.99)	NR	100		**Younger: 51.2 (14.3)** Older: 48.0 (11.3)		
Butler and Montgomery (48)	15 AN	27.9 (9.9)	NR	100	I_7	15.40 (2.61)	NA	NA
	16 HC	28.4 (8.3)	22.75	100		14.19 (2.74)		
Calderoni et al. (49)	32 AN	14.78 (1.75)	15.07 (1.54)	100	IRI	5.13 (6.98)	**0.44 (6.87)**	4.69 (7.08)
	41 HC	14.02 (1.69)	NR	100		9.44 (5.66)	**5.24 (6.45)**	4.20 (4.75)
Courty et al. (50)	15 AN	23.9 (4.7)	16.4 (1.7)	93.33	EQ-short	23.0 (6.8)	NR	NR
					IRI	70.8 (4.83)	34.1 (4.85)	36.7 (4.8)
	15 HC	24.0 (4.9)	21.0 (1.8)	93.33	EQ-short	21.1 (7.4)	NR	NR
					IRI	73.09 (3.79)	38.3 (3.31)	35.6 (4.22)
	15 ASD	28.1 (7.5)	23.2 (5.0)	13.33	EQ-short	10.1 (5.7)	NR	NR
					IRI	65.5 (4.77)	32.6 (4.73)	32.9 (4.81)
	15 HC	28.1 (7.3)	22.2 (3.0)	13.33	EQ-short	19.9(3.4)	NR	NR
					IRI	67.0 (3.39)	34.7 (2.75)	32.3 (3.93)
Duchesne et al. (51)	60 BED	NR	38.1	100	IRI	81.4 (4.04)	42.4 (4.40)	39.0 (3.65)
	60 obese controls	NR	37.9	100		81.3 (3.95)	42.7 (3.36)	38.6 (4.46)
	54 HC	NR	21.4 (1.6)	100		80.6 (4.02)	43.4 (4.30)	37.2 (3.72)
Feldman and Eysenck (52)	45 BN	25.13 (6.59)	NR	100	I_7	14.73 (3.17)	NA	NA
	761 HC	NR	NR	100		14.39 (2.87)		
Gramaglia et al. (53)	39 AN	30.59 (3.0)	16.3	NR	IRI	82.93 (3.81)	41.19 (4.48)	41.74 (2.99)
	48 HC	33.19 (3.37)	21.82	100		80.48 (3.78)	41.9 (4.15)	38.58 (3.37)
Guttman and Laporte (54)	28 AN	22	NR	100	IRI	72.7 (5.60)	35.1 (5.51)	37.6 (5.69)
	26 BPD	32	NR	100		78.9 (5.45)	34.7 (5.56)	44.2 (5.35)
	27 HC	21	NR	100		71.9 (4.83)	35.9 (4.61)	36 (5.04)
Harnbrook et al. (55)	22 AN	26.73 (4.77)	15.27 (1.22)	100	EQ	45.9 (12.5)	NR	NR
	45 HC	32.51 (9.63)	23.36 (3.76)	100		46.2 (11.1)		
Jermakow and Brzezicka (56)	11 AN	26.80 (4.3)	NR	100	EQ	44.60 (8.58)	NR	NR
					IRI	**63.10 (3.39)**	34.9 (6.22)	28.2 (4.46)
	33 female HC	21.33 (1.4)	NR	100	EQ	42.42 (9.84)	NR	NR

(Continued)

TABLE 1 | Continued

References	Group	Mean age (SD)	Mean BMI (SD)	% female	Empathy measure	Mean (SD) total empathy	Subscales reported?	
							Mean (*SD*) cognitive empathy	Mean (*SD*) affective empathy
					IRI	**70.03 (2.13)**	*38.52 (4.40)*	*31.52 (4.40)*
	10 ASD	28.30 (9.5)	NR	0	EQ	30.00 (5.05)	NR	NR
					IRI	57.90 (2.20)	*33.5 (5.59)*	*24.4 (3.64)*
	27 male HC	21.76 (2.0)	NR	0	EQ	32.63 (9.97)	NR	NR
					IRI	62.70 (2.33)	*33.38 (5.60)*	*29.33 (5.21)*
Lüle et al. (57)	15 AN	16.2 (1.26)	17.07 (1.44)	100	IRI	121.14 (11.25)	NR	NR
	15 HC	16.5 (1.09)	21.06 (1.57)	100		118.50 (10.20)		
Morris et al. (58)	28 AN	26.3 (7.9)	15.5 (1.3)	100	SEQ	**18.8 (2.5)**	NA	NA
	25 AN-REC	29.5 (9.2)	20.1 (1.9)	100		19.8 (3.0)		
	54 HC	29.4 (9.6)	23.1 (3.9)	100		**20.4 (2.4)**		
Nandrino et al. (59)	23 AN	19.64 (1.82)	15.2 (1.07)	100	BES	79.57 (6.70)	35.57 (3.45)	44.00 (5.44)
	23 HC	20.65 (1.90)	21.05 (1.78)	100		80.78 (6.04)	36.78 (3.19)	44.00 (4.93)
Peres et al. (60)	41 AN	16.2 (1.4)	79.78 (8.71) %IBW	100	IRI	*74.44 (4.30)*	35.5 (6.99)	**39.0 (6.45)**
	38 HC	15.84 (1.83)	100.5 (11.71) %IBW	100		*73.1 (4.1)*	37.6 (7.18)	**35.6 (5.21)**
Redondo and Herrero-Fernandez(61)	38 AN	21.9 (5.30)	NR	100	EQ-short	23.42 (7.25)	11.26 (4.84)	7.11 (2.68)
					IRI††	NR	NR	NR
	321 HC	NR	NR	100	EQ-short	25.79 (7.21)	11.03 (4.63)	7.55 (2.35)
					IRI††	NR	NR	NR

Significant differences between ED and HCs are indicated in bold. Italics indicate where scores were not reported in the study, but could be calculated from subscale scores. Potential significant differences could therefore not be reported for calculated scores. AN, anorexia nervosa; AN-REC, recovered anorexia nervosa; ASD, autism spectrum disorder; BED, binge eating disorder; BES, Basic Empathy Scale; BMI, body mass index; BN, bulimia nervosa; BPD, borderline personality disorder; EQ, Empathy Quotient; HC, healthy control; I7, Impulsiveness, Venturesomeness, and Empathy questionnaire; IRI, Interpersonal reactivity index; NA, not applicable; NR, not reported; SD, standard deviation; SEQ, Socio-Emotional Questionnaire.

† Groups were split into groups depending on age and EQ version used.

†† Only the PT subscale of the IRI was used.

Data Analysis

All analyses were performed using R Studio (39) using the metafor package (40). Cohen's d was used to estimate effect sizes and is reported with 95% confidence intervals (CIs). Effect sizes are interpreted using Cohen's (41) definitions of small (0.2), medium (0.5), and large (0.8). Negative effect sizes indicate lower empathy scores in the ED group compared to HC. Separate meta-analyses were performed for different components of empathy. Where two measures of empathy were used in the same study (and therefore on the same group of participants), a multivariate meta-analysis was performed using the rma.mv command. Between-study heterogeneity was calculated using Cochran's Q test. Where heterogeneity was found ($p < 0.05$), meta-regressions were performed using age and empathy measure as moderators.

Risk of Bias

Publication bias was assessed through visual inspection of funnel plots, where the absence of studies in the bottom right corner indicates publication bias. The symmetry of the funnel plots was formally assessed using Begg's rank correlation test (42). Publication bias was also assessed using Rosenthal's fail-safe N (43), which estimates the number of unpublished studies required to change the significant effect size into a non-significant one.

Risk of bias in individual studies was assessed using the Clinical Appraisal Skills Programme checklist for case–control studies (44). The checklist considers how methodological features of studies may have impacted the results, e.g., exclusion and inclusion criteria, recruitment sources, and whether potential confounding variables were included in analyses. Studies can receive a maximum score of 17.

RESULTS

Study Characteristics

Study characteristics are shown in **Table 1**. Fourteen of the included studies compared AN and HC groups. Of these studies, one study also included a recovered AN group, two included an ASD group, and one included a group with BPD. Two studies compared those with binge eating disorder (BED) to HC, and one study compared participants with BN to HC.

In total, 6 different self-report measures were used across studies, with the Interpersonal Reactivity Index [IRI; (62)] being used most often (9 studies). The IRI comprises of four subscales: perspective taking (PT; the tendency to spontaneously adopt the psychological viewpoint of others), fantasy (FS; the tendency to identify oneself with fictional characters in books, plays and movies), empathic concern (EC; assesses "other-oriented" feelings of sympathy and concern for others), and personal distress (PD; assesses "self-oriented" feelings of anxiety and unease in tense interpersonal settings). Cognitive and affective empathy scores can be calculated by taking the sum of PT and FS, and EC and PD respectively. The Empathy Quotient [EQ; (6)], and the EQ-short (63) were used in seven studies, and both have three subscales: cognitive empathy, affective empathy, and social skills. Other measures used were: the empathy subscale of the Impulsiveness, Venturesomeness, and Empathy questionnaire (I_7; (64) (2 studies), the empathy subscale of the Socio-Emotional Questionnaire [SEQ; (65)] (1 study), and the Basic Empathy Scale [BES; (66)] (1 study). One study used two different versions of the EQ depending on participants' age; the parent reported version for younger adolescents, and the self-report version for older adolescents (47). Only the self-report scores are included in the meta-analysis, as this was the focus of the present review.

Methodological quality of the studies varied considerably (range: 7–16). None of the studies reported a power calculation, and sample sizes were generally small (ranging from 11 to 66 in ED groups). All but one study (46) matched participants on at least one characteristic, most often sex. The mean age of participants ranged from 14.02 to 50.60 years, although three studies did not report the mean age of at least one participant group (51, 52, 61). Seven studies did not report mean BMI or percentage IBW in at least one participant group (47–49, 52, 54, 56, 61). Most studies used exclusively female samples, however three studies included male participants (46, 50, 56).

Synthesized Findings

Only studies comparing AN and HC could be included in meta-analyses, due to too few studies with other ED groups (2 BED, 1 BN). The number of studies in each meta-analysis is displayed in **Figure 2**.

Total Empathy

Fourteen studies were included in a meta-analysis comparing total empathy scores in AN and HCs. The random effects model with a total sample size of 2165 participants (AN = 379, HC =

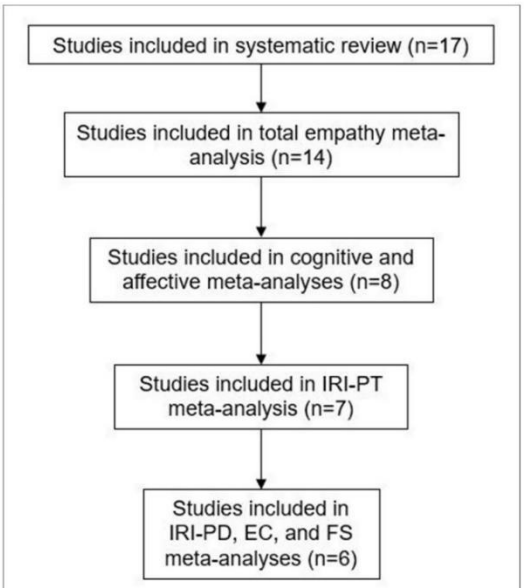

FIGURE 2 | Studies included in the review and meta-analyses.

1746) revealed that total empathy scores in AN did not differ from those of HCs [$d = -0.11$, (95% CI −0.36, 0.13) $z = -0.92$, $p = 0.36$] (**Figure 3**).

There was evidence of significant heterogeneity across studies [$Q_{(15)} = 79.61$, $p < 0.001$], therefore meta-regressions with age and empathy measure as moderator variables were performed. The moderators explained a significant amount of the variance [$QM_{(6)} = 27.88$, $p = < 0.001$], however no single factor had a significant influence on the size of the effect. The test for residual heterogeneity was significant [$QE_{(8)} = 65.08$, $p = < 0.001$].

Cognitive Empathy

Eight studies were included in a meta-analysis comparing cognitive empathy scores in AN and HC. The random effects model with at total sample size of 773 participants (AN = 227, HC = 546) revealed that cognitive empathy scores in AN were significantly lower than HCs [$d = -0.34$, (95% CI −0.58, −0.11) $z = -2.86$, $p = 0.004$] (**Figure 4**). There was no evidence of significant heterogeneity [$Q_{(7)} = 12.27$, $p = 0.09$].

Affective Empathy

Eight studies were included in a meta-analysis comparing affective empathy scores in AN and HC. The random effects model with a total sample size of 773 participants (AN = 227, HC = 546) revealed that affective empathy scores in AN did not differ from those of HCs [$d = 0.18$, (95% CI −0.17, 0.52) $z = 1.01$, $p = 0.31$] (**Figure 5**).

There was evidence of significant heterogeneity across studies [$Q_{(7)} = 26.99$, $p < 0.001$], therefore meta-regressions with age and empathy measure as moderator variables were performed. The moderators did not explain a significant amount of the variance [$QM_{(3)} = 0.64$, $p = 0.88$], and the test for residual heterogeneity was significant [$Q_{(4)} = 17.6$, $p = 0.002$].

Risk of Bias

The funnel plots for total empathy, cognitive empathy, and affective empathy scores are displayed in **Figures 6–8**. There was no evidence of publication bias in the total empathy meta-analysis (Begg's test $p = 0.45$), however there was evidence of publication bias in the studies included in the cognitive empathy meta-analysis (Begg's test $p = 0.03$, Rosenthal's fail safe $N = 38$). Studies included in the affective empathy meta-analysis did not show any evidence of publication bias (Begg's test $p = 0.40$).

Additional Analyses

Because several studies reported on the PT, FS, EC, and PD subscales of the IRI, additional meta-analyses were performed to test for differences between AN and HC. Six studies reported scores for all four subscales, while one additional study reported PT scores only. The results are shown in **Table 2**. AN had significantly lower FS scores compared to HC, however there were no significant differences in the other sub-scales. There was no evidence of significant heterogeneity in any of the subscale meta-analyses, nor was there significant evidence of publication bias (Begg's test all $p > 0.05$) (see **Supplementary Material** for subscale forest and funnel plots).

Qualitative Findings

Studies in AN

Studies using the EQ or the EQ-short reported very mixed findings. Adenzato et al. (45) found that those with AN had significantly lower total EQ scores compared to HCs. In adolescents, this was only found to be true for those aged 12–15years, using the parent report version of the EQ (47). The older AN group did not differ from age-matched HC on the self-report EQ. Redondo and Herrero-Fernández (61) found that while total EQ-short scores in those with AN and HCs did not differ, those with AN scored significantly lower than HCs on the social skills subscale. Three studies found no differences in EQ scores between AN and HC, however both groups scored significantly higher than those with ASD (50, 55, 56).

Results from studies using the IRI were similarly mixed. Only two studies tested for group differences in total IRI scores, with one reporting significantly lower scores in those with AN than HCs (56) and the other reporting no differences (57). Two studies tested for group differences in cognitive and affective empathy sub-scores of the IRI. Cognitive empathy scores are calculated by summing the F and PT subscale scores together, while the EC and PD subscale scores are summed to calculate affective empathy scores. Calderoni et al. (49) found that those with AN had significantly lower cognitive empathy scores, whereas Peres et al. (60) reported significantly higher emotional empathy scores in AN compared to HC.

Six studies reported on group differences between AN and HCs on IRI EC, PD, FS, and PT (with one additional study included the PT subscale only). Regarding EC, there were no significant differences between AN and HC across all six studies (49, 50, 53, 54, 56, 60). However, those with AN had significantly higher EC scores compared to those with ASD (50), and significantly lower scores than women with BPD (54). Two studies found that those with AN scored higher on PD than HC (53, 60), while one reported that AN and ASD groups had lower scores than HCs (56). Three studies reported no differences in PD scores between AN and HC, however those with BPD had higher scores than both AN and HC groups (49, 50, 54). Regarding the FS subscale, it was found that those with AN had significantly lower scores than HC, similar to those with ASD (49, 50). However, four studies did not find significant differences between groups (53, 54, 56, 60). Calderoni et al. (49) and Redondo and Herrero-Fernandez (61) reported that AN had significantly lower PT scores compared to HCs, however the remaining five studies found no significant differences (50, 53, 54, 56, 60).

The remaining AN studies used the I_7, the empathy subscale of the SEQ, and the BES. Morris et al. (58) found that AN scored significantly lower on the SEQ than HC. Scores in the recovered AN group did not differ from either group, lying between the two. The remaining two studies found no significant differences between AN and HCs (48, 59). However, both studies were limited in their sample sizes (15 and 23 participants in the clinical groups respectively), and therefore there may not be sufficient power to detect group differences.

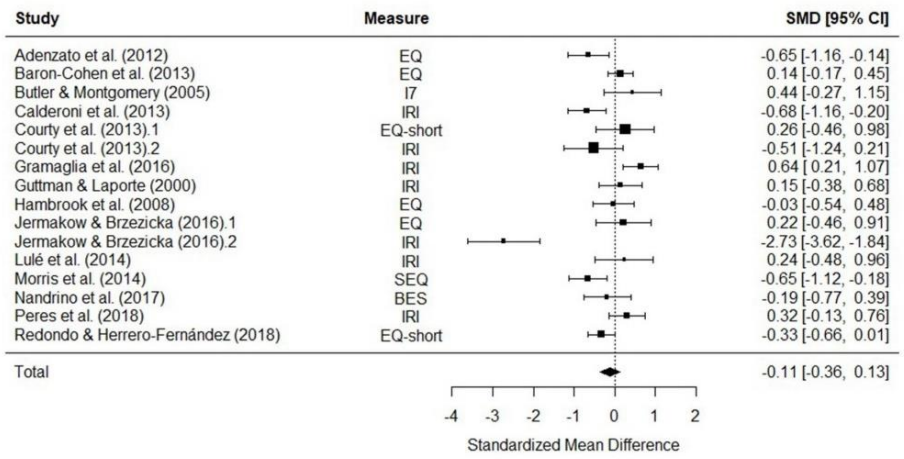

FIGURE 3 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on total empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; I_7, Impulsiveness, Venturesomeness, and Empathy questionnaire; IRI, interpersonal reactivity index; SEQ, Socio-Emotional Questionnaire.

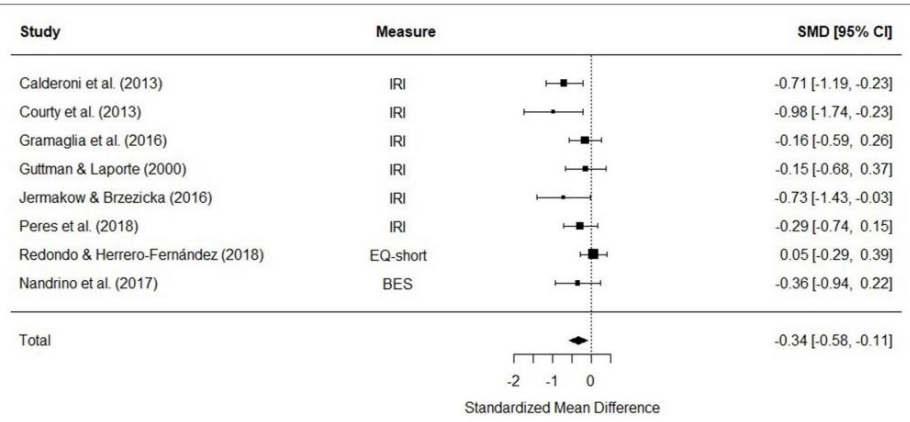

FIGURE 4 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on cognitive empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; IRI, interpersonal reactivity index.

Studies in Other EDs

Only three studies involved participants with BED or BN. Feldman and Eysenck (52) reported no differences in empathy scores between women with BN and HCs. However, this study had the poorest methodological quality rating of all studies include in the review, mainly because it included little information about the HC group, and did not control for any confounding variables. In BED, total empathy scores did not significantly differ across those with BED, subthreshold BED, and HCs (46). However, 51 reported that women with BED scored significantly higher than obese and HC women on the PD subscale of the IRI. Further, a logistic regression revealed that lower PT and higher PD scores were associated with BED. Unfortunately, this study did not control for confounding variables such as depression, which has been found to be associated with PD (9).

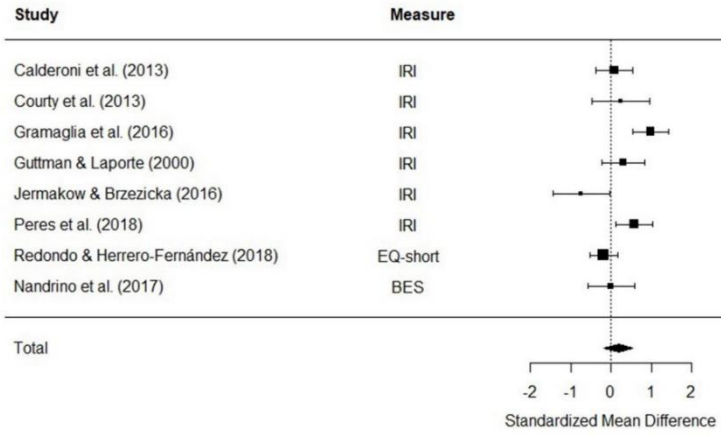

FIGURE 5 | Forest plot of standardized mean effect size for differences (SMD) between anorexia nervosa (AN) and healthy controls (HC) on affective empathy scores. Negative effect sizes indicate lower empathy scores in the AN group. BES, Basic Empathy Scale; CI, confidence interval; EQ, empathy quotient; IRI, interpersonal reactivity index.

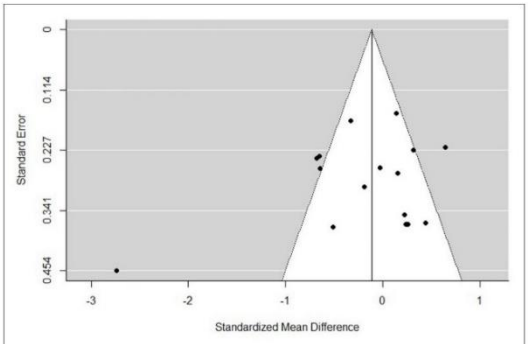

FIGURE 6 | Funnel plot of studies included in the total empathy meta-analysis.

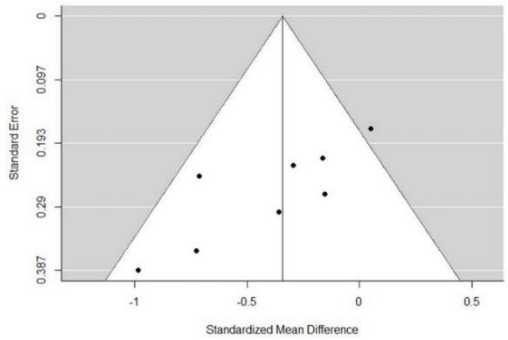

FIGURE 7 | Funnel plot of studies included in the cognitive empathy meta-analysis.

Associations With Psychopathology and Clinical Variables

Few studies examined associations between empathy and clinical variables or other measures of psychopathology. In BED and AN, negative correlations were found between EQ and alexithymia scores on the twenty-item Toronto Alexithymia Scale [TAS-20; (67)], such that lower levels of empathy were associated with higher alexithymia (45, 46). The latter study also found that higher EQ scores were associated with more social support in AN, as measured by the Multidimensional Scale of Perceived Social Support [MSPSS; (68)]. Only two studies examined whether empathy was associated with ED psychopathology and illness severity in AN. Baron-Cohen et al. (47) reported that EQ scores were not associated with scores on the Eating Disorder Examination Questionnaire [EDEQ; (69)], and Calderoni et al. (49) found that cognitive empathy scores were not associated with BMI, disease duration, or general psychopathology in AN. Finally, Peres et al. (60) reported that IRI, AE and PD subscale scores were positively associated with anxiety, but not depression, as measured by the Hospital Anxiety and Depression Scale [HADS; (70)]. However, linear regressions revealed that anxiety did not explain the differences in empathy between AN and HC better than group membership.

DISCUSSION

Summary of Main Findings

The aim of this review was to examine group differences in empathy in those with EDs compared to HC, and provide a

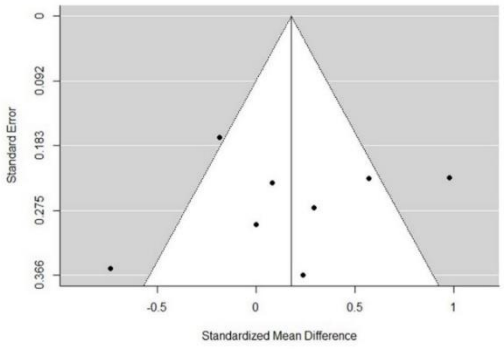

FIGURE 8 | Funnel plot of studies included in the total affective meta-analysis.

qualitative synthesis of the literature. Meta-analyses were run for total empathy, cognitive empathy, affective empathy, and four further sub-components of empathy: PT, FS, EC, and PD. There were no significant differences between those with AN and HC in overall empathy (14 studies) or affective empathy scores (8 studies). However, it was found that those with AN had significantly lower cognitive empathy scores compared to HC (8 studies), with a small effect size. Further, it those with AN had significantly lower FS scores than HC (6 studies), with a small effect size, but did not significantly differ from HC on any of the other IRI subscores.

The finding that AN have lower cognitive empathy abilities compared to HC is in accordance with studies examining related, performance-based measures of empathy, such as ToM (32), emotion recognition (31), and emotional intelligence (71). Affective empathy has been less well-studied in EDs, although it appears from this review, and a few experimental studies, that individuals with ED are not impaired in affective empathy. For example, one study found that those with BN reported higher levels of sadness than restrained eaters and HCs in response to video clip, during which they were asked to identify themselves with the protagonist whose boyfriend leaves them for an attractive woman (72). Another study examined individuals' own emotional reactions to video clips depicting an individual displaying emotion, finding that the intensity of the emotions experienced by those with EDs (AN and BN) did not differ from HC (73). However, those with EDs did show less facial expressivity while watching the clips—a component of empathy that has been termed "motor empathy" (74). Studies that utilize physiological measurements of empathy, such as facial electromyographic activity (EMG), skin conductance, and heart rate may be useful in further understanding affective empathy in EDs.

There are a number of possible explanations for the dissociation between cognitive and affective empathic abilities found here. Distinct brain systems for cognitive and affective empathy have been described: the ventromedial prefrontal cortex is involved in cognitive empathy, while the inferior frontal gyrus is involved in affective empathy (75). Neuroimaging studies have reported differences in the ventromedial prefrontal cortex in those with AN (76, 77), thus providing a possible explanation for lowered cognitive empathy abilities. fMRI studies utilizing performance-based measures of empathy could be useful in testing this hypothesis. Relatedly, difficulties in executive functioning are reported in those with AN and BN (78). Since executive functions contribute to the development of cognitive empathy (79), it would be of interest to determine whether there is a relation between empathy abilities and executive functioning in those with EDs. Relatedly, it might be that reduced attention to faces and eyes found in AN (28, 80, 81) leads to decreased cognitive empathy abilities.

There was evidence of significant heterogeneity in the overall empathy and affective empathy studies. While age and empathy measurement did explain some of the variance in total empathy scores, no single factor had a significant influence on the size of the effect. Due to a lack of studies reporting on factors such as BMI and illness duration, it was not possible to include these indicators of illness severity as moderators. The two studies that did examine potential associations between ED severity and empathy did not find any significant relationships (47, 49). Research examining the relationship between illness severity and constructs related to empathy such as mentalizing (the ability to understand the mental states of oneself or others, and how such states might influence behavior) have been mixed. While some have reported independence from BMI and illness length (82), a meta-analysis found that poorer performance on the RMET was associated with longer illness duration (83). Examining whether cognitive or affective empathy are state or trait variables will be important in characterizing the socio-emotional phenotype proposed for EDs (84).

Relatedly, it would be of interest to examine whether other psychopathological variables may have influenced the effect sizes reported in this review. One candidate is ASD symptoms. Support for this idea comes from a longitudinal population-based study which examined mentalizing abilities in those with AN and HCs (21), in which 29% of the AN group also met criteria for a diagnosis of ASD. They found that when mentalizing ability was compared between AN+ASD, AN only, and HCs, only the AN+ASD group had significantly lower scores than HC. Thus, it is possible that there is a sub-group of individuals with AN who display the most severe difficulties in socio-emotional measures, whose difficulties are missed when assessing group differences. While ASD symptoms could not be included as moderators in the meta-analyses presented here, it would be important to ascertain whether reduced empathy in AN is a characteristic of the ED, or some other comorbid psychopathology.

Alternatively, it could be the case that the heterogenous results in AN might be explained by alexithymia. Indeed, a few studies included in this review found that lower levels of empathy in AN and BED were associated with higher alexithymia (45, 46). Alexithymia is a subclinical phenomenon characterized by difficulties in describing and recognizing one's own emotions, and distinguishing feelings from bodily sensations of emotional arousal. "Shared network" models of empathy propose that the networks in the brain responsible for processing one's own

TABLE 2 | Statistical outcomes for meta-analyses of the four IRI subscales.

IRI subscale	N studies	Pooled AN sample N	Pooled HC sample N	Cohen's *d*	95% CI	*Z*	*p*
Perspective taking	7	204	523	−0.2	−0.44, 0.05	−1.59	0.11
Fantasy	6	166	202	**−0.41**	−0.62, −0.20	3.83	**>0.001**
Empathic concern	6	166	202	0.01	−0.20, 0.22	1.1	0.92
Personal distress	6	166	202	0.3	−0.13, 0.74	1.36	0.17

Significant differences between AN and HCs are indicated in bold. AN, anorexia nervosa; CI, confidence intervals; HC, healthy control; IRI, Interpersonal Reactivity Index.

emotions are the same networks used to represent the emotions of others (85–87). Thus, it is possible that the high levels of alexithymia experienced by those with AN might be responsible for lower levels of empathy compared to HCs. In support of this hypothesis, an fMRI study in ASD showed that the strength of empathic brain responses in the left anterior insula were predictive of degree of alexithymia in both ASD and HCs, but did not vary as a function of group (88). The potential contribution of alexithymia to reduced empathy, and indeed other aspects of socio-emotional functioning in EDs, should be explored.

Only two studies examined empathy in BED, finding no difference in total empathy scores, but significantly higher PD scores compared to HCs (46, 51). The finding that those with BED experience more stress and unease in tense social settings is consistent with literature documenting emotion regulation difficulties in those with BED, and it is hypothesized that binge eating may be a strategy to deal with increased negative emotions (89). It would therefore be of interest to examine whether higher PD scores in BED are associated with more severe ED psychopathology. The only study that measured empathy in BN found no significant differences in empathy compared to HCs (52). This study used the I_7 to measure empathy, and therefore no study has yet examined cognitive and affective components of empathy in BN. Clearly, the lack of studies in BN and BED prevent any conclusions being made regarding empathy in these groups. Given that problems with interpersonal functioning are a prominent feature in BN (18, 90), research using multidimensional measures of empathy in this population are needed.

The findings from the current review have implications for treatment of AN. Socio-communicative and interpersonal problems are associated with poorer outcomes (20, 21, 82, 91, 92) and more severe ED psychopathology (36, 37), therefore socio-emotional functioning may be a potential target for the development of new, more holistic treatment approaches. For example, group social skills interventions are effective in improving communication, social anxiety, and social functioning in those with ASD (93, 94). There is also evidence to suggest that Cognitive Remediation and Emotion Skills Training (CREST), an intervention designed to improve emotion processing, is effective in decreasing alexithymia and social anhedonia, while increasing motivation in those with AN (95, 96). Recently, there has also been interest in exploring the effect of oxytocin, a hormone implicated in prosocial behavior, on socio-emotional functioning (97, 98). In ASD, administration of intranasal oxytocin has been found to increase interactions with socially cooperative peers, and enhance feelings of trust (99). Oxytocin also increased participants' attention to the eyes of pictures of faces, avoidance of which is a core feature of ASD (100). A few studies have examined the effect of oxytocin on socio-emotional cognition in those with EDs. One study found intranasal oxytocin increased emotion recognition and decreased calorie consumption in those with BN, however no effects were seen in AN (101). Another found no effect of oxytocin on RMET performance in AN (102). However, whether oxytocin has an effect on real-life social behavior in those with EDs has yet to be examined.

Limitations

Several limitations of this review should be noted. Firstly, many studies did not report empathy subscale scores, and therefore could not be included in affective and cognitive empathy meta-analyses. Secondly, although this method has been employed in previous reviews of this type (103, 104), it could be questioned whether it is appropriate to compare different scales that purport to measure the same empathy constructs. For example, the affective subscales of the IRI have been criticized as more closely reflecting sympathy, as they focus on reactions to others, rather than emotion matching (105). However, studies in this review generally included the most widely used measures of empathy (e.g., the EQ and the IRI), and as previously noted, empathy measure did not significantly influence effect sizes in moderator analyses.

It is also important to note the limitations of self-report empathy measures generally. Socially desirable responding may be an issue with self-report measures, as they do not objectively measure empathic abilities, but rather how empathetic individuals perceive themselves to be. In other psychiatric disorders, a discrepancy between performance-based empathy tasks and self-report measures has been reported. For example, a meta-analysis found that people with schizophrenia display greater affective empathy deficits in performance-based tasks than on self-report measures (103). If affective empathy partly relies on one's ability to report on their own emotional reactions, this might be especially difficult in populations with high levels of alexithymia, such as AN (106).

The number of studies in other EDs, such as BN and BED, was greatly lacking. Therefore, meta-analyses for group differences between these groups and HCs could not be carried out. Furthermore, only three studies included males with EDs, thus the results from this review cannot be generalized to this population. Interestingly, it is reported that while males with EDs (AN, BN, or eating disorder not otherwise specified) show the same difficulties in cognitive flexibility and weak central coherence often found in women with EDs, they do not differ

from HC men in terms of ToM performance or sensitivity to social threat (107). Future work should therefore examine performance in a broader range of socio-emotional tasks in order to understand possible similarities and differences in the male and female presentations of EDs.

Finally, there was evidence of publication bias in the cognitive empathy meta-analysis, indicating that studies with non-significant results may have been missing from analyses. However, the fact that the affective empathy meta-analysis, which included the same studies as the cognitive meta-analysis, did not show any evidence of publication bias and showed a non-significant result, perhaps lends support to the validity of our findings. Nonetheless, the results should be interpreted with caution.

CONCLUSIONS

Although there is an extensive literature documenting difficulties in ToM and emotion recognition in those with EDs, relatively little is known about empathic abilities in this population. This systematic review and meta-analysis aimed to examine whether those with EDs differed from HCs on several dimensions of self-reported empathy, and provide a qualitative synthesis of the literature. While those with AN did not differ from HCs in overall empathy, a meta-analysis of 8 studies found that AN had significantly lower levels of cognitive empathy compared to HC, with a small effect size. It was also found that AN had significantly lower levels of fantasy, a subdivision of cognitive empathy. AN did not differ from HC in affective empathy. This profile of intact affective empathy and lowered cognitive empathy mirrors that of those with ASD, a disorder that shares a number of neuropsychological and socio-cognitive traits with AN. Conclusions regarding the empathic profiles of those with other EDs are not possible, given the lack of studies in these groups. Future research should investigate empathic abilities in other EDs, and examine the influence of comorbid psychopathological traits.

AUTHOR CONTRIBUTIONS

JK-G performed the search, data extraction, and wrote the manuscript. KT leads the research group within which this work was conducted and is JK-G lead supervisor for Ph.D. KT and AH edited the manuscript before submission.

ACKNOWLEDGMENTS

JK-G is supported by the Economic and Social Research Council (ESRC). KT would like to acknowledge support from MRC and MRF Child and Young Adult Mental Health (Grant no: MR/R004595/1) and Prof Tracey Wade and Norman Munn Distinguished Visiting Scholar Award 2017/2018 from Flinders University South Australia. AH would like to acknowledge support from the MRC.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00102/full#supplementary-material

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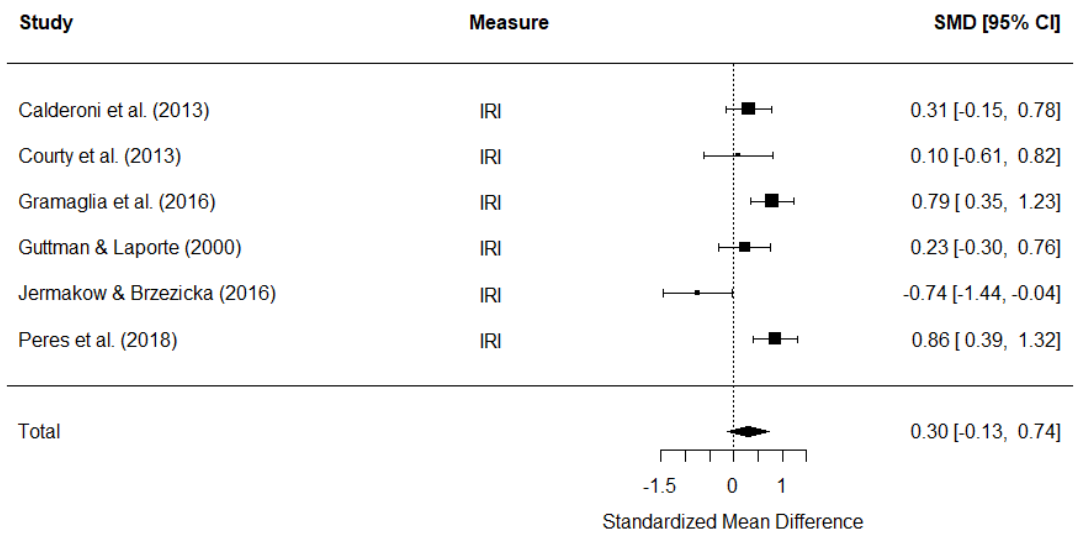
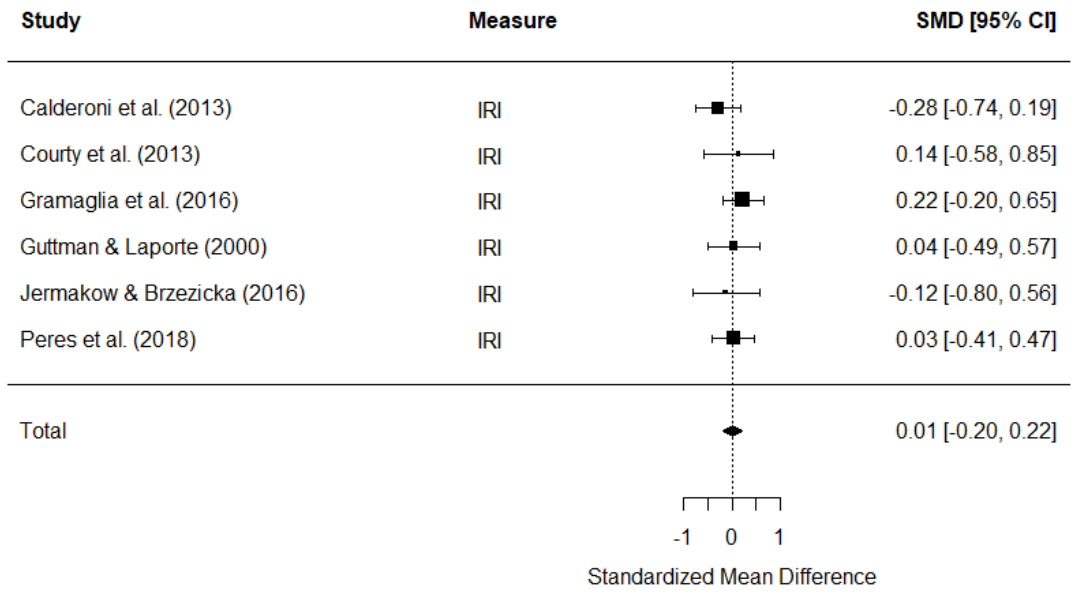
Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

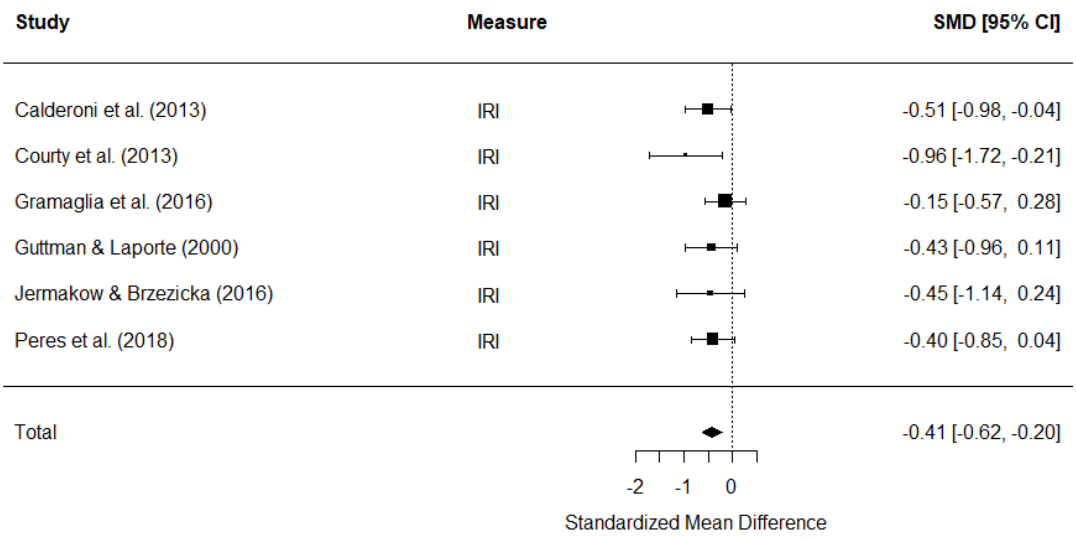
7.1 Supplementary material



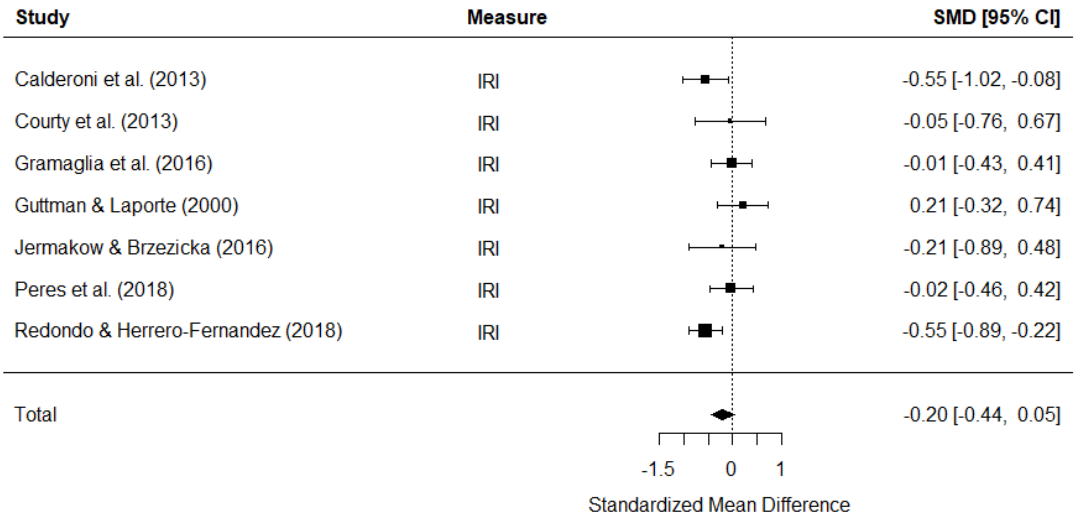
Supplementary figure 1. Forest plot of standardized mean effect size for differences (SMD) between AN and HC on the personal distress subscale of the IRI. Negative effect sizes indicate lower empathy scores in the AN group.



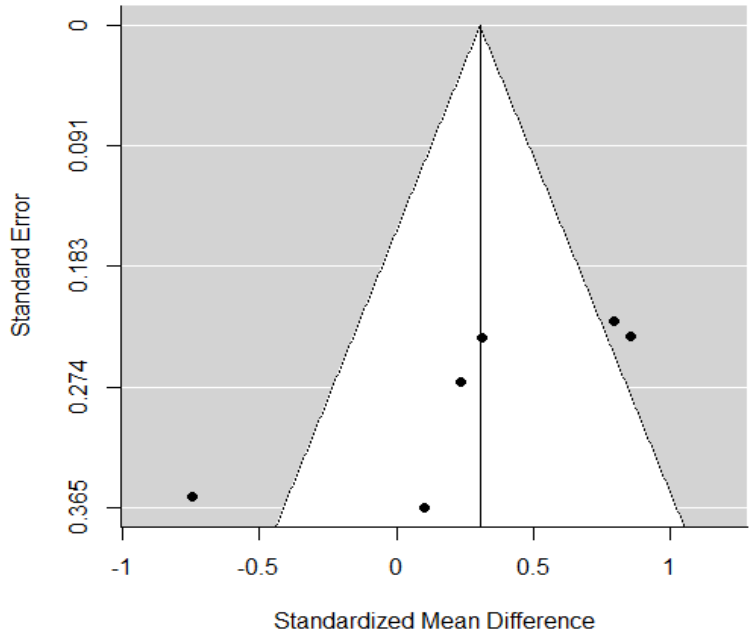
Supplementary figure 2. Forest plot of standardized mean effect size for differences (SMD) between AN and HC on the empathic concern subscale of the IRI. Negative effect sizes indicate lower empathy scores in the AN group.



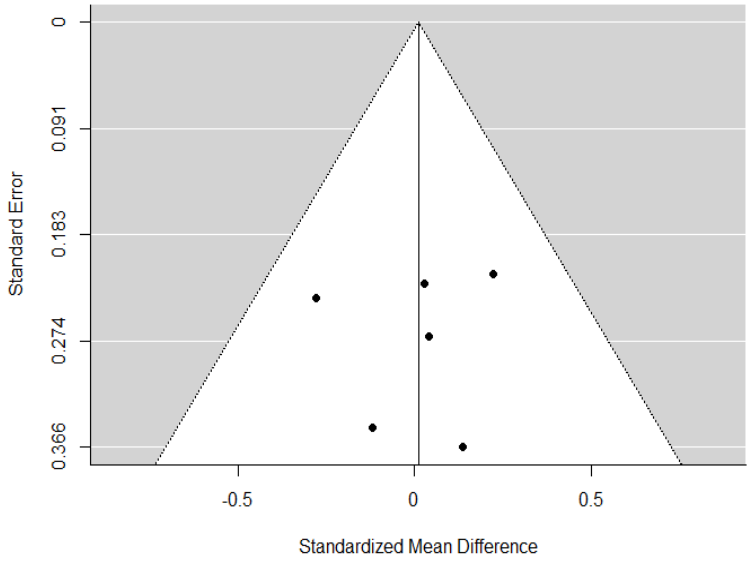
Supplementary figure 3. Forest plot of standardized mean effect size for differences (SMD) between AN and HC on the fantasy subscale of the IRI. Negative effect sizes indicate lower empathy scores in the AN group.



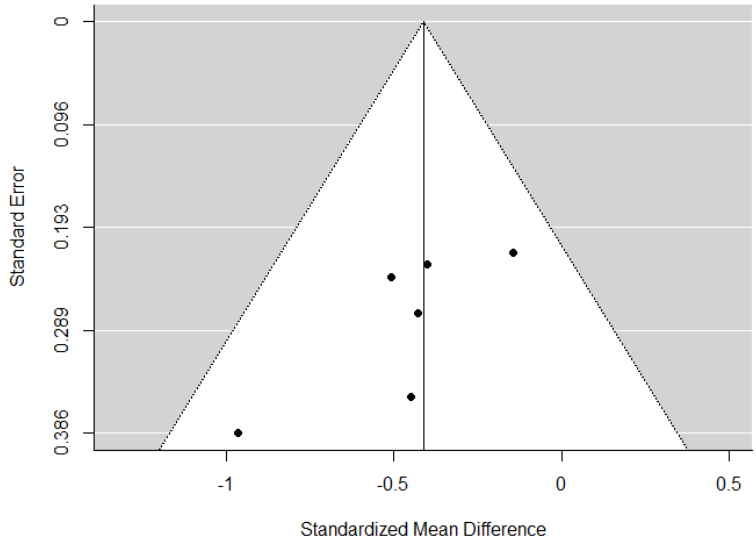
Supplementary figure 4. Forest plot of standardized mean effect size for differences (SMD) between AN and HC on the perspective taking subscale of the IRI. Negative effect sizes indicate lower empathy scores in the AN group.



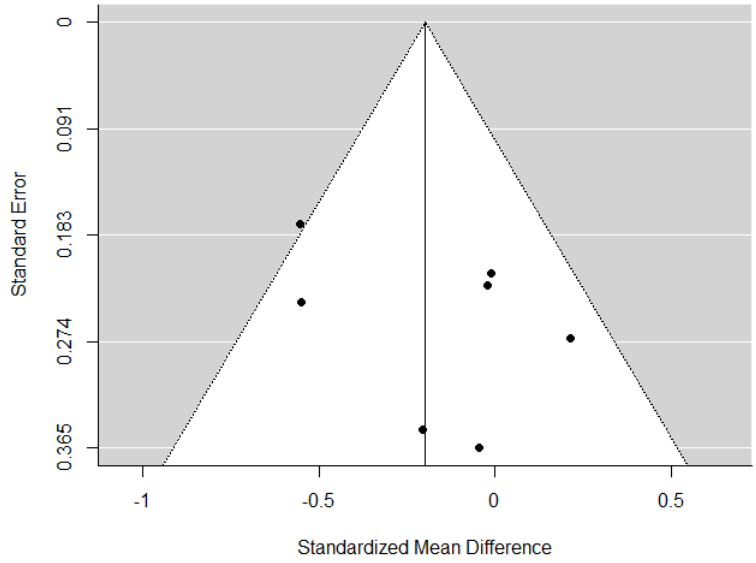
Supplementary figure 5. Funnel plot of personal distress subscale scores to assess publication bias (p = 0.06).



Supplementary figure 6. Funnel plot of empathic concern subscale scores to assess publication bias (p = 1.00).



Supplementary figure 7. Funnel plot of fantasy subscale scores to assess publication bias (p = 0.06).



Supplementary figure 8. Funnel plot of perspective taking subscale scores to assess publication bias (p = 0.77).

7.2 Studies published after the review

Since the publication of this review, two studies examining empathy in individuals with AN have been published. Nalbant et al. (2019) used the KA-SI Empathic Tendency Scale-Adolescent form (Kaya & Siyez, 2010) to compare empathic abilities in adolescents with AN and HCs. Total, affective, and cognitive empathy scores were significantly lower in the AN group compared to HCs, however these differences did not remain significant after controlling for depression, anxiety, childhood trauma, and attachment security. In the second study, Konstantakopoulos et al. (2020) found that AN and BN showed significantly lower EQ total scores compared to HCs, with BN showing the lowest scores. Interestingly, difficulties in cognitive functioning (visuospatial ability, working memory, and set-shifting) were found to account for lower scores on the EQ in individuals with AN, but not in those with BN. Further, lower empathy scores were associated with higher BMI in individuals with AN, and higher bulimic symptoms in individuals with BN. There were no differences across groups in affective empathy, however individuals with BN showed lower cognitive empathy scores than AN and HC.

Chapter 8 - Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa

Kerr-Gaffney, J. E., Harrison, A., & Tchanturia, K. (2020). Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa. *Journal of Affective Disorders, 266*, 273-281. https://doi.org/10.1016/j.jad.2020.01.169

8.1 Abstract

Background: Social and emotional difficulties have been identified as key factors in the development and maintenance of anorexia nervosa (AN). However, few studies have investigated the influence of comorbid psychopathology on social cognition. The aim of the current study was to examine perception of nonverbal communication and empathy in AN using ecologically valid, performance-based measures, and to explore associations with comorbid psychopathology (anxiety, depression, autism spectrum disorder (ASD) traits, alexithymia, and social anxiety). **Methods**: In this cross-sectional study, the Multifaceted Empathy Test (MET) and the Mini Profile of Nonverbal Sensitivity (MiniPONS) were administered to 51 adults with AN, 51 recovered AN (REC), and 51 healthy controls (HCs). Comorbid psychopathological traits were assessed using self-report questionnaires and the Autism Diagnostic Observation Schedule – 2nd edition (ADOS-2). **Results**: Individuals with AN showed reduced affective empathy to positive stimuli compared to HCs, and a trend towards lower vocal prosody recognition scores relative to REC. Around a quarter of AN and REC scored above the clinical cut-off for ASD on the ADOS-2, and high ASD symptoms predicted lower cognitive and affective empathy scores. **Limitations**: The study is cross-sectional, future research would benefit from examining social-cognition performance and comorbid psychopathology longitudinally. **Conclusions**: The findings highlight the importance of ASD symptoms in empathy dysfunction in those with a lifetime history of AN. Future research should explore whether treatment adaptations to accommodate for differences in social-cognitive abilities may be helpful in the treatment of AN.

Key words: anorexia nervosa, empathy, emotion recognition, ASD, comorbidity

8.2 Introduction

Contemporary models of eating disorders (EDs) such as anorexia nervosa (AN) suggest social and emotional difficulties are key factors in the development and maintenance of the disorder (Treasure & Schmidt, 2013). During the illness, a variety of social difficulties are seen, including social anxiety (Kerr-Gaffney et al., 2018), poorer social skills (Rhind et al., 2014; Winecoff et al., 2015), and less social support (Tiller et al., 1997). Given that interpersonal problems are associated with more severe ED psychopathology (Illing et al., 2010; Tasca et al., 2011) and poorer outcomes (Franko et al., 2013; Gillberg et al., 1994; Jones et al., 2015; Zipfel et al., 2000), it is important to understand possible underlying mechanisms. One area that has received considerable attention is emotion recognition, an aspect of theory of mind (ToM). Those with AN show difficulties in recognising emotions and inferring the mental states of others, compared to healthy controls (HCs) (Bora & Kose, 2016). Individuals with AN may also have difficulties in other aspects of ToM, such as understanding social interactions and implicit social attribution, however research in this area is lacking (Leppanen et al., 2018).

The majority of emotion recognition studies in AN have used static images restricted to the face or eye region only (Leppanen et al., 2018). Consequently, much of the information that is inherent in everyday social interactions, such as tone of voice, body language, and context is missing from such stimuli. Research has therefore investigated emotion recognition using different modalities of nonverbal communication in order to better understand the mechanisms that may underlie social difficulties in AN. For example, a few studies have examined emotion recognition from body movements or voice only. Individuals with AN were less accurate at recognising sadness but better at recognising anger conveyed through body movements compared to weight-restored AN and HCs (Lang et al., 2015; Zucker et al., 2013). However group differences became nonsignificant after controlling for BMI in one study (Zucker et al., 2013). AN were also less accurate than HCs at recognising emotions conveyed through voice (Kucharska-Pietura et al., 2004; Oldershaw et al., 2010). Again, group differences were not significant in one study

when covariates (age, education, depression) were controlled for. Finally, a few studies have examined perception of nonverbal behaviour more holistically, using paradigms that include facial expression, posture, and vocal prosody together. For example, Gramaglia et al. (2016) used the Awareness of Social Inference Test (TASIT; McDonald et al., 2002), finding no significant differences between individuals with AN and HCs in identifying emotional states from video clips. However, the clips involved speech, therefore the task cannot be considered a pure measure of nonverbal communication only. Thus, the limited research available suggests there may be differences in perception of nonverbal communication in those with AN, however further exploration of the impact of various clinical factors, such as anxiety, depression, and BMI is required.

Relatedly, there is some evidence to suggest there are differences in empathy in AN. Empathy is considered a key component of prosocial behaviour and social cognition, as it allows us to make sense of and respond appropriately to others' behaviour (Decety et al., 2016; Eisenberg & Miller, 1987). It comprises two major facets: cognitive and affective empathy. While cognitive empathy refers to the ability to recognise and understand the mental states of others (overlapping with the concept of ToM); affective empathy is the ability to share the feelings of others, without any direct emotional stimulation to oneself (Blair, 2005). Based on longitudinal research in a community sample, Gillberg and colleagues reported on a subgroup of participants with AN with "empathy disorders." This group had severe problems in social understanding and communication, consistent with a diagnosis of autism spectrum disorder (ASD) (Gillberg et al., 1994). Poorer outcomes in terms of recovery and psychosocial functioning were found in this group (Anckarsäter et al., 2012; Wentz et al., 2009). More recently, several studies have used self-report measures to investigate empathy in AN. A meta-analysis of these studies reported that while overall empathy and affective empathy did not differ between AN and HC, those with AN had significantly lower cognitive empathy scores (Kerr-Gaffney et al., 2019). However, self-reported measures of empathy are limited in that they measure how empathetic individuals perceive themselves to be, rather than providing an objective measure of performance.

In those with EDs, only two studies have used a performance-based or "online" measure of empathy. Both studies found no significant differences between ED and HC groups in empathic ratings to videos or in an empathy for pain paradigm (Cardi et al., 2015; Brewer et al., 2019). However, the latter study demonstrated that high levels of alexithymia were associated with increased empathic personal distress (Brewer et al., 2019). These studies both used mixed ED samples (AN and BN), limiting the generalisability of the results for either of the two disorders, and only affective empathy was assessed. Importantly, the study by Brewer et al. (2019) demonstrates that comorbid traits such as alexithymia may explain differences in emotion processing, rather than the ED itself. Indeed, other studies in EDs have shown that alexithymia rather than ED diagnosis predicts emotion recognition abilities (Brewer et al., 2015). Thus, it is possible that the mixed results in emotion processing studies in EDs are due to samples differing in their levels of alexithymia, such that when alexithymia is particularly high in the ED group (or low in the HC group) a group difference is found.

Several other comorbid traits may influence socio-emotional cognition in AN in this way. For example, between 4 and 52.5% of individuals with AN show high ASD traits – scoring above clinical thresholds on diagnostic interviews for ASD (Anckarsäter et al., 2012; Vagni et al., 2016; Westwood et al., 2018; Westwood et al., 2017). Individuals with ASD show difficulties in ToM (Happé, 1994; Kleinman et al., 2001), emotion recognition (Bal et al., 2010; Harms et al., 2010; Hubert et al., 2007), empathy (Baron-Cohen & Wheelwright, 2004; Kok et al., 2016), and social attention (Chita-Tegmark, 2016). Further, ASD traits in the general population are associated with more difficulties in these areas (Blain et al., 2017; Halliday et al., 2014; Luo et al., 2017; Zhao et al., 2018). Therefore, it is possible that high levels of ASD traits co-occur with socio-emotional processing difficulties in a proportion of those with AN. Although a few studies have found associations between high ASD traits and more severe socio-emotional difficulties, such as alexithymia (Westwood et al., 2017), social anhedonia (Adamson et al., 2018), and flattened facial affect (Lang, Larsson, et al., 2016), research exploring the effect of ASD traits on social cognition performance in AN is lacking. Anckarsäter et al. (2012) assessed ToM performance using the Happé

cartoon task, comparing those with AN who also met criteria for ASD (AN+ASD) to those who did not (AN-ASD), as well as HCs. HCs were significantly more accurate on the mental cartoons task than AN+ASD, whereas performance in the AN-ASD group did not significantly differ from either of the other two groups, lying in the middle.

The aim of this experimental study was to examine cognitive and affective empathy and perception of nonverbal communication in AN, recovered AN (REC), and HCs. A secondary aim was to explore potential relationships between comorbid psychopathological traits and performance on social cognition tasks. As well as including measures of the aforementioned ASD traits and alexithymia, we included depression, anxiety, and social anxiety, due to their high co-occurrence with AN (Kerr-Gaffney et al., 2018; Pollice et al., 1997; Swinbourne & Touyz, 2007) and potential effects on social cognition (Attwood et al., 2017; Bourke et al., 2010; Demenescu et al., 2010; Hezel & McNally, 2014; Schreiter et al., 2013; Washburn et al., 2016).

Based on previous literature documenting difficulties in self-reported cognitive empathy (Kerr-Gaffney et al., 2019), we hypothesised that individuals with AN would show poorer cognitive empathy performance compared to HCs, but no differences in affective empathy. We expected an intermediate cognitive empathy profile in REC (scores lying between that of AN and HC). Regarding perception of nonverbal communication, we hypothesised that AN would show lower overall performance compared to HCs. We did not make any prediction on the specific modalities affected, due to a lack of research in this area.

8.3 Methods

8.3.1 Participants

Ethical approval was obtained from the National Health Service Research Ethics Committee (Camberwell St Giles, 17/LO/1960). All participants were required to be between 18 and 55 years old and fluent in English. Exclusion criteria were a history of brain trauma or learning disability. HC participants were recruited through a King's College London email circular and posters around campuses. Before taking part, HC

participants were screened using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV; First et al., 2015), to ensure they did not meet criteria for any psychiatric disorders. HCs were required to have a body mass index (BMI) between 19 and 27.

In addition to the university advertisements, participants with AN or REC were recruited through online advertisements (B-eat, call for participants, MQ mental health). Participants with AN were also recruited through two specialist NHS ED services in London. AN and REC were screened using the SCID-5-RV to confirm a current or past diagnosis of AN. Participants with AN were required to have a BMI ≤ 18.5, and REC participants a BMI between 19 and 27. Further, REC participants were required to have maintained a BMI within this range for at least one year prior to testing.

8.3.2 Materials

The Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II; Wechsler, 2011) measures verbal intelligence and perceptual reasoning, as well as full-scale IQ. The two subtest version was used (vocabulary and matrix reasoning).

The Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994) measures severity of ED psychopathology. Global scores are calculated by averaging responses across items, with higher scores indicating more severe symptoms (max 6). HCs with a score of >2.7 were excluded to ensure those with possible sub-threshold ED symptoms were not included (Lang, Larsson, et al., 2016). Cronbach's alpha was 0.98.

The Autism Diagnostic Observation Schedule – 2nd edition (ADOS-2), Module 4 (Lord et al., 2012) is a standardised semi-structured interview for the assessment of ASD. It includes a range of questions and activities designed to evoke behaviours and cognitions associated with ASD. The revised algorithm, which was designed to more closely reflect the DSM-5 criteria for ASD was used for scoring (Hus & Lord, 2014). The algorithm has two subscales: social affect and restrictive and repetitive behaviours, and total scores of 8 or more indicate possible ASD. The ADOS-2 was used

in this study to provide an observational measure of ASD traits, which is recommended in the assessment of ASD (National Institute for Clinical Excellence [NICE], 2012). Interviews were administered and scored by the first author, who received ADOS-2 training and met requirements for research reliability.

The Social Responsiveness Scale-2nd Edition, adult self-report form (SRS-2; Constantino & Gruber, 2012) measures symptoms associated with ASD, with higher scores (max 195) indicating more autistic symptoms. There are five subscales: social awareness, social cognition, social communication, social motivation, and restrictive interests and repetitive behaviour. Cronbach's alpha was 0.97.

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) is a 14-item scale with two subscales: anxiety and depression. Subscale scores are interpreted as: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21). Cronbach's alpha was 0.94.

The Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987) has two subscales: fear and avoidance of social situations. A score of 60 has been established as a cut-off indicative of social anxiety disorder (Rytwinski et al., 2009). Cronbach's alpha was 0.97.

The twenty-item Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994) has three subscales: difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking. Total scores range from 0 to 100, and cut-offs are as follows: ≤51 = no alexithymia; 52-60 = borderline alexithymia; and ≥61 = alexithymia (Parker et al., 1993). Cronbach's alpha was 0.90.

The Work and Social Adjustment Scale (WSAS; Mundt et al., 2002) is a brief measure of functional impairment in five domains: work, home management, social leisure, private leisure, and ability to form and maintain close relationships. Scores range from 0 to 40, with a score of 20 or more indicating clinical significance. Cronbach's alpha was 0.93.

The Multifaceted Empathy Test (MET; Dziobek et al., 2008) is a performance-based measure of cognitive and affective empathy, using photo-realistic, context-embedded stimuli. Forty photographs of people in various emotional states (20 positive and 20 negative) are presented twice. In 40 trials participants are asked to identify which emotion the person is feeling out of a choice of four emotions (cognitive empathy), and in a further 40 trials they are asked to indicate how much they empathise with the person depicted on a scale of 1 (*not at all*) to 9 (*a lot*) (affective empathy). The outcome measure for cognitive empathy is a total correct score out of 40 (although note that scores in normative samples do not reach ceiling, e.g., Drimalla et al., 2019; Kuypers et al., 2017), while affective empathy is a mean score out of 9. Positive and negative empathy scores can be calculated for affective and cognitive empathy. The MET was presented on a 14" monitor using Psychopy (Pierce, 2009).

The Mini-Profile of Nonverbal Sensitivity (MiniPONS; Bänziger et al., 2011) measures the ability to recognise emotions, interpersonal attitudes, and intentions from different modes of nonverbal communication (face only, body only, voice only, face and voice together). The task consists of 64 clips (2s each), depicting the same actor in different interpersonal situations. Respondents are required to indicate the correct answer from a choice of two after each clip. The short version used here correlates highly with the full version, which has been validated in a number of populations (Rosenthal et al., 1979). A total score out of 64 is calculated, as well as scores out of 16 for each of the four channels. Accuracy in a normative sample in the original validation study was 80% for total scores (Bänziger et al., 2011).

8.3.3 Procedure

Participants attended a testing session at the Institute of Psychiatry, Psychology & Neuroscience, however where participants were inpatients (n = 11), testing took place at their place of treatment. Written informed consent was obtained. The first author administered the WASI-II, followed by the MET and the MiniPONS, and then conducted the ADOS-2. Finally the participant completed the questionnaires. At the end of the session, participants' heights and weights were taken to calculate BMI

(weight/height^2). The session took around 2 hours, and all participants were reimbursed £20 for their time.

8.3.4 Data analysis

Histograms and Q-Q plots were inspected to check for normal distributions. Where variables were positively skewed, a logarithmic transformation was applied. Homogeneity was assessed using Levene's test. Group differences in social cognition, psychopathology, and demographic information were assessed using one-way ANOVAs and Tukey's post-hoc tests, or Welch's ANOVA with Games-Howell post-hoc tests where the assumption of homogeneity was violated. Independent samples *t*-tests were used when assessing group differences between AN and REC only. Chi-squared tests of homogeneity (or Fisher's exact test where the sample size assumption was not met) were conducted for dichotomous variables.

Pearson's correlations were run to explore potential relationships between psychopathology (EDE-Q, HADS anxiety, HADS depression, LSAS, SRS-2, TAS-20, WSAS, and ADOS-2 total scores), demographic variables (age, IQ, BMI, age at diagnosis, illness length), and performance on social cognition tasks. Where significant correlations were found, hierarchical linear regressions were run to examine whether dimensions of psychopathology predicted social cognition performance, after controlling for associated demographic variables and group membership.

8.4 Results

8.4.1 Demographic information

One hundred and fifty-three participants were recruited. Out of 51 HCs, five were excluded based on their EDE-Q scores, and one REC participant was excluded due to BMI >27. Thus, 46 HCs, 51 AN and 50 REC participants were included in analyses. Demographic information is presented in Table 1. Groups were of similar age, gender, and IQ. As expected, AN had a significantly lower BMI than both REC and HC (both p <.001). Age at diagnosis was significantly older in individuals with AN compared to

REC, and they were more likely to be taking a psychiatric medication. Seventy-eight percent of participants with AN had a diagnosis of AN restricting sub-type (AN-R), the rest had AN binge-purge subtype (AN-BP). AN-R and AN-BP did not differ on any demographic variable or performance on social-cognitive tasks, however AN-BP had significantly higher HADS depression scores, $t(49) = -2.08$, $p = .043$ and TAS-20 scores, $t(31.55) = -2.16$, $p = .038$.

8.4.2 Psychopathology

Scores on self-report questionnaires assessing dimensions of psychopathology and functional impairment are presented in Table 2, as well as ADOS-2 total and subscale scores. On each self-report scale, all three groups significantly differed from one another, with AN showing the highest levels of psychopathology, REC an intermediate profile, and HC the lowest scores. Regarding the ADOS-2, AN had significantly higher total, SA, and RRB scores than HCs (all $p < .01$). A significantly higher proportion of AN and REC participants scored above the clinical cut-off for ASD compared to HC (both $p < .05$).

8.4.3 Social cognition

Results from the MET and MiniPONS are presented in Table 3. Groups did not significantly differ in their total cognitive empathy scores or mean affective empathy. However, AN had significantly lower positive affective empathy scores compared to HC ($p = .004$). Groups did not differ on total MiniPONS scores, however an ANOVA revealed perception of nonverbal communication through voice significantly differed between groups. Post hoc tests indicated a trend towards AN scoring lower than REC, $p = .057$.

Table 1. Mean (*SD*) demographic information

	AN (*N* = 51)	REC (*N* = 50)	HC (*N* = 46)	Test statistics	*p*-value	ηp²/*d*
Age (years)[†]	27.57 (8.52)	26.33 (8.04)	24.37 (4.43)	*F*(2, 92.29) = 2.50	.09	.03
% female	92.2	98.0	93.5	Fisher's exact test = 1.89	.44	
BMI	15.72 (1.41)[a]	21.20 (1.95)[b]	21.69 (1.88)[b]	*F*(2, 143) = 178.44	**<.001**	.71
Years of education	16.22 (3.15)	16.53 (2.59)	16.63 (2.45)	*F*(2, 143) = 0.42	.66	.01
IQ	109.69 (13.28)	109.66 (11.28)	113.78 (7.25)	*F*(2, 143) = 2.16	.12	.03
Age diagnosed[†]	19.64 (7.22)[a]	16.44 (3.53)[b]	-	*t*(83.56) = 2.70	**.01**	.56
Illness length (years)	7.19 (7.45)	5.31 (5.62)	-	*t*(90.92) = 1.63	.11	.28
% on psychiatric medication	54.9[a]	32.0[b]	-	X^2 = 5.39	**.02**	

AN, anorexia nervosa; BMI, body mass index; HC, healthy control; IQ, intelligence quotient; REC, recovered anorexia nervosa; SD, standard deviation.

Different superscripts indicate significant differences between groups, significant *p*-values are highlighted in bold.

[†]Variable was log transformed for analyses, original values are displayed.

Table 2. Mean (*SD*) scores on self-report questionnaires and ADOS-2

	AN (*N* = 51)	REC (*N* = 50)	HC (*N* = 46)	Test statistics	*p*-value	ηp²
EDE-Q	3.85 (1.37)[a]	1.82 (1.51)[b]	0.61 (0.58)[c]	*F*(2, 80.38) = 118.73	**<.001**	.54
HADS anxiety	13.92 (4.46)[a]	10.78 (5.07)[b]	5.02 (3.09)[c]	*F*(2, 93.61) = 71.10	**<.001**	.42
HADS depression	10.14 (4.31)[a]	5.00 (3.99)[b]	1.54 (1.68)[c]	*F*(2, 83.47) = 92.50	**<.001**	.50
LSAS	71.68 (31.41)[a]	56.60 (29.86)[b]	27.91 (18.32)[c]	*F*(2, 91.43) = 41.29	**<.001**	.31
SRS-2	85.29 (32.78)[a]	70.04 (31.97)[b]	39.23 (20.18)[c]	*F*(2, 138) = 30.44	**<.001**	.30
TAS-20	58.82 (13.28)[a]	49.80 (14.92)[b]	37.47 (11.26)[c]	*F*(2, 139) = 32.37	**<.001**	.30
WSAS	23.26 (8.70)[a]	11.10 (8.6)[b]	3.59 (6.23)[c]	*F*(2, 93.6) = 79.93	**<.001**	.51
ADOS						
Total	5.47 (4.44)[a]	4.18 (4.46)[ab]	2.70 (2.52)[b]	*F*(2, 91.23) = 7.86	**<.001**	.88
SA	4.71 (4.03)[a]	3.74 (3.93)[ab]	2.50 (2.38)[b]	*F*(2, 92.34) = 5.95	**.004**	.78
RRB	0.76 (1.07)[a]	0.44 (0.88)[ab]	0.20 (0.58)[b]	*F*(2, 92.35) = 5.65	**.005**	.82
% above cut-off	27.5[a]	24[a]	4.3[b]	X^2 = 9.58	**.008**	

ADOS-2, Autism Diagnostic Observation Schedule – 2nd edition; AN, anorexia nervosa; EDE-Q, eating disorder examination questionnaire; HADS, hospital anxiety and depression scale; HC, healthy control; LSAS, Liebowitz Social

Anxiety Scale; REC, recovered anorexia nervosa; RRB, restrictive and repetitive behaviours; SA, social affect; SD, standard deviation; SRS-2, social responsiveness scale-2nd edition; TAS-20, Twenty-item Toronto Alexithymia Scale; WSAS, Work and Social Adjustment Scale

Different superscripts indicate significant differences between groups, significant *p*-values are highlighted in bold.

Table 3. Mean (*SD*) social cognition scores and analysis of group differences

	AN (*N* = 51)	REC (*N* = 50)	HC (*N* = 46)	Test statistics	*p*-value	ηp²
MET cognitive empathy (max 40)	27.22 (3.55)	28.42 (3.01)	27.72 (3.49)	*F*(2, 143) = 0.72	.49	.01
Positive (max 20)	15.00 (1.90)	15.15 (2.03)	15.20 (1.98)	*F*(2, 143) = 0.14	.87	.00
Negative (max 20)	12.72 (2.41)	13.22 (1.84)	12.52 (2.43)	*F*(2, 143) = 1.26	.28	.02
MET affective empathy (max 9)	4.74 (1.67)	4.90 (1.32)	5.30 (1.66)	*F*(2, 143) = 1.65	.20	.02
Positive (max 9)	3.84 (1.99)[a]	4.41 (1.68)[ab]	5.10 (1.99)[b]	*F*(2, 143) = 5.34	**.006**	.07
Negative (max 9)	5.63 (1.93)	5.40 (1.52)	5.50 (2.01)	*F*(2, 143) = 0.21	.81	.00
MiniPONS total (max 64)	48.27 (7.31)	50.43 (4.21)	49.61 (4.22)	*F*(2, 92.91) = 1.69	.19	.03
Face only (max 16)	11.53 (1.94)	11.80 (1.50)	11.61 (1.45)	*F*(2, 143) = 0.34	.71	.01
Body only (max 16)	12.04 (1.97)	12.10 (1.56)	11.72 (1.76)	*F*(2, 143) = 0.64	.53	.01
Voice only (max 16)	11.88 (2.62)	12.86 (1.49)	12.71 (2.03)	*F*(2, 143) = 3.13	**.047**	.04
Face & voice (max 16)	12.82 (2.46)	13.67 (2.01)	13.57 (1.46)	*F*(2, 92.99) = 1.08	.13	.04

AN, anorexia nervosa; HC, healthy control; MET, multifaceted empathy test; MiniPONS, Mini-Profile of Nonverbal Sensitivity; REC, recovered anorexia nervosa; SD, standard deviation

Different superscripts indicate significant differences between groups, significant *p*-values are highlighted in bold.

8.4.4 Associations between psychopathology and social cognition

Cognitive empathy scores were significantly positively associated with IQ (r = .29, p <.001) and age (r = .22, p = .009), and negatively correlated with ADOS-2 (r = -.29, p <.001), SRS-2 (r = -.23, p = .005), and TAS-20 scores (r = -.20, p = .02). A hierarchical multiple regression was run to determine if the addition of ADOS-2 and TAS-20 scores would improve the prediction of cognitive empathy scores over group membership, age, and IQ.[1] The full model was significant, R^2 = .20, F(6, 132) = 5.37, p <.001, adjusted R^2 = .16. Details of each regression model are displayed in Table 4. The addition of ADOS-2 scores to the prediction of cognitive empathy (Model 2) led to a significant increase in R^2 of .04, F(1, 133) = 6.48, p = .012. The addition of TAS-20 scores (model 3) did not significantly add to the prediction.

Table 4. Hierarchical regression analysis predicting cognitive empathy from associated demographic variables and psychopathology scores

	Model 1	Model 2	Model 3
IQ	.29***	.25**	.24**
Age[†]	.20*	.18*	.16*
ADOS-2		-.21*	-.18*
TAS-20			-.12
R^2	.15	.19	.20

Note: Figures shown are standardised coefficients. Group membership was entered in Model 1, but was not significant and not displayed here

[†]Variable was log transformed for analyses

*p <.05

** p <.01

*** p <.001

[1] SRS-2 scores were not included in regressions due to the correlation with ADOS-2 scores

Mean affective empathy was significantly positively correlated with BMI (r = .17, p = .042), and negatively correlated with WSAS (r = -.23, p = .006), HADS anxiety (r = -.24, p = .004), HADS depression (r = -.26, p = .002), LSAS (r = -.22, p = .009), TAS-20 (r = -.35, p <.001), SRS-2 (r = -.37, p <.001), and ADOS-2 total scores (r = -.30, p <.001). A hierarchical multiple regression was run to determine if the addition of ASD symptoms, HADS anxiety and depression, LSAS, and TAS-20 scores would improve the prediction of affective empathy scores over group membership and BMI.[2] The full model was significant, R^2 = .18, F(7, 132) = 4.03, p <.001, adjusted R^2 = .13. Details of each regression model are displayed in Table 5. The addition of ADOS-2 scores to the prediction of cognitive empathy (Model 2) led to a significant increase in R^2 of .08, F(1, 135) = 12.42, p = .012. The addition of HADS (model 3), TAS-20 (Model 4), and LSAS scores (Model 5) did not significantly add to the prediction.

Table 5. Hierarchical regression analysis predicting affective empathy from associated demographic variables and psychopathology scores

	Model 1	Model 2	Model 3	Model 4	Model 5
BMI	.31*	.26	.23	.20	.19
ADOS-2		-.30***	-.26**	-.22*	-.23*
HADS			-.21	-.10	-.14
TAS-20				-.21	-.23
LSAS					.09
R^2	.05	.13	.15	.17	.18

Note: Figures shown are standardised coefficients. Group membership was entered in Model 1, but was not significant and not displayed here

*p <.05

** p <.01

*** p <.001

[2] WSAS scores were not included in regressions due to the hypothesised direction of causality between variables.

Total MiniPONS scores were positively correlated with BMI (r = .21, p = .01) and IQ (r = .27, p = .001), and negatively correlated with WSAS (r = -.19, p = .026), HADS depression (r = -.20, p = .019), SRS-2 (r = -.29, p =.001), and ADOS-2 (r = -.21, p = .011). A hierarchical multiple regression was run to determine if the addition of ADOS-2 scores and HADS depression would improve the prediction of MiniPONS scores over group membership, BMI, and IQ. The full model was significant, R^2 = .12, F(6, 134) = 2.90, p = .011, adjusted R^2 = .08. See Table 6 for details of each regression model. The addition of ADOS-2 scores (model 2) and HADS depression (model 3) did not significantly add to the prediction of MiniPONS scores.

Table 6. Hierarchical regression analysis predicting MiniPONS scores from associated demographic variables and psychopathology scores

	Model 1	Model 2	Model 3
BMI	.26	.26	.25
IQ	.28***	.27**	.26**
ADOS-2		-.04	-.03
HADS depression			-.12
R^2	.11	.11	.12

Note: Figures shown are standardised coefficients. Group membership was entered in Model 1, but was not significant and not displayed here

*p <.05

** p <.01

*** p <.001

Associations between ASD symptoms and cognitive and affective empathy were explored further by grouping individuals with lifetime AN (REC and current AN) based on whether they met the clinical cut-off for ASD on the ADOS-2, and comparing their scores with HCs. The two HCs who scored above cut-off on the ADOS-2 were excluded, due to their being too few cases to assess group differences. Thus, 44 HC, 26 lifetime AN scoring above ADOS-2 cut-off (AN+ASD), and 75 lifetime AN scoring below the ADOS-2 cut off (AN-ASD) were included in analyses. Results are displayed

in Figure 1. One-way ANOVAs with Tukey's post-hoc tests indicated that AN+ASD had significantly lower total cognitive empathy and positive cognitive empathy scores compared to AN-ASD (p = .015 and p = .019 respectively). AN+ASD also had significantly lower mean affective empathy scores than AN-ASD (p = .011) and HC (p = .003), and lower positive affective empathy scores than AN-ASD (p = .049) and HC (p <.001). AN-ASD and HC did not significantly differ on any of the MET outcome measures.

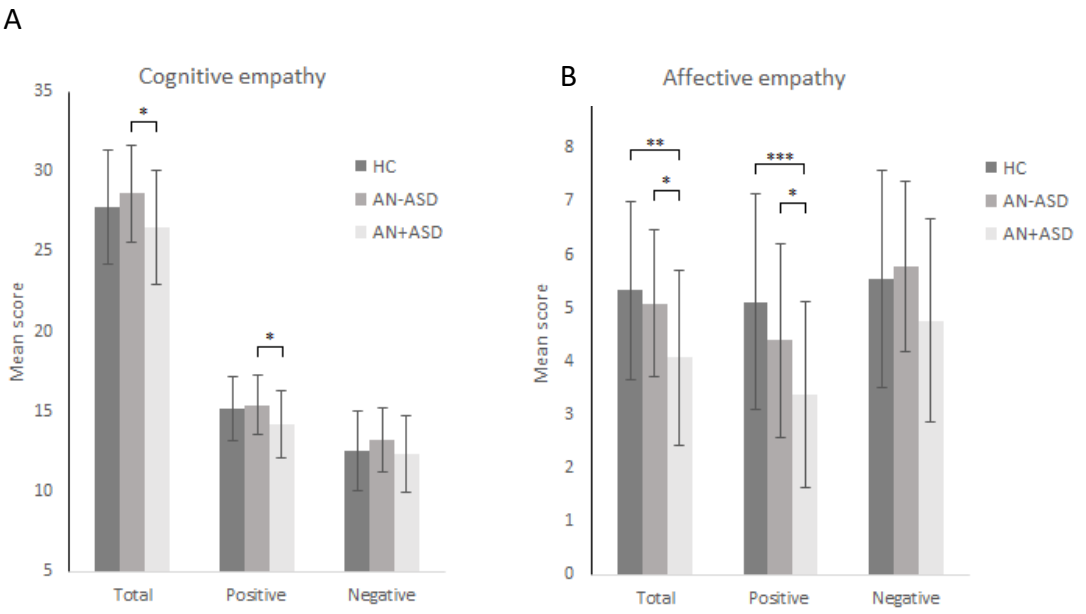


Figure 1. Mean scores for A) cognitive empathy and B) affective empathy. Error bars indicate standard deviation. HC = healthy controls; AN-ASD = lifetime AN, below cut-off on the ADOS-2; AN+ASD = lifetime AN, above cut-off on the ADOS-2. Significant p-values indicating group differences are marked with an asterisk; * <.05, ** <.01, *** <.001.

8.5 Discussion

The primary aim of the current study was to compare performance across socio-emotional cognition tasks in individuals with AN, recovered AN, and HCs. To our knowledge, this is the first study to use a performance-based measure of cognitive and affective empathy in AN. Contrary to our hypothesis, there were no differences in cognitive empathy across groups. Instead, those with AN showed significantly lower affective empathy performance when stimuli were positively valanced,

compared to HC. Performance in the REC group reflected an intermediate profile and did not significantly differ from that of the other two groups. Regarding perception of nonverbal behaviour, no significant group differences in total MiniPONS scores were found. However, there was a trend towards lower vocal prosody perception scores in AN relative to REC. In addition, associations between social cognition performance, dimensions of psychopathology, and demographic variables were found. Each of these findings will be discussed in turn.

The lack of group differences in cognitive empathy contrasts with findings from a recent meta-analysis, which found that individuals with AN had lower self-reported cognitive empathy scores (small effect size) compared to HC (Kerr-Gaffney et al., 2019). Discrepancies between self-report and performance-based measures of empathy have been found in other psychiatric disorders, such as schizophrenia (Bonfils et al., 2016; Derntl et al., 2009). Self-reporting one's own empathic abilities may be particularly difficult in those with high levels of alexithymia, as was the case in our AN group. Our results also contrast with previous studies showing emotion recognition difficulties in AN (Caglar-Nazali et al., 2014). There are a number of possible explanations for this. The MET, while showing relatively complex emotional states, also includes contextual information (e.g., a woman looking tired in a hospital bed). Thus, the cognitive empathy test in the MET does not measure pure emotion recognition ability from isolated facial expressions. A tentative conclusion may be that while individuals with AN have some difficulties in recognising emotions from faces alone, they are able to attend to other cues in the environment that facilitate understanding and empathising ability.

Another explanation for the lack of group differences in cognitive empathy (and overall affective empathy) scores concerns another of our findings: ASD symptoms predicted empathic abilities, rather than AN diagnosis. The correlation analysis showed that higher cognitive empathy scores were associated with higher IQ and older age, and lower levels of alexithymia and ASD symptoms (measured by both the ADOS-2 and SRS-2). When entered into regression models, IQ, age, and ADOS-2 scores remained as significant predictors of cognitive empathy scores. Higher affective empathy scores were correlated with higher BMI, and lower levels of

anxiety, depression, social anxiety, alexithymia, ASD symptoms (measured by both the SRS-2 and ADOS-2) and work and social adjustment difficulties. However, when entered into the regression model, only ADOS-2 scores significantly predicted affective empathy scores. Further, individuals with lifetime AN who scored above the clinical cut-off on the ADOS-2 (AN+ASD) had lower overall and positive cognitive empathy scores, compared to those who scored below the cut-off (AN-ASD). AN+ASD also had lower overall affective empathy and positive affective empathy scores than both AN-ASD and HCs, who did not differ from one another on any empathy measure. Thus, it is possible that variations in ASD symptoms across study samples contribute to the mixed findings in emotion recognition and empathy studies in AN. It must be noted that R^2 was rather small in our regression analyses, suggesting other unmeasured factors also contributed to empathic abilities.

Despite ASD symptoms being a better predictor of overall affective empathy, individuals with AN had lower positive affective empathy scores compared to HCs. This is in agreement with a few studies investigating facial expressivity – a component of empathy that has been termed *motor empathy* (Blair, 2005). Two studies found that those with AN produced fewer positive facial expressions in response to a positive film clip compared to HC, whereas there was no difference between groups while watching negatively valanced clips (Cardi, Corfield, et al., 2014; Lang, Larsson, et al., 2016). Although not included in our study, previous research using the MET has found that affective empathy scores are strongly associated with degree of facial expressivity during the task (Drimalla et al., 2019). Difficulties in empathising with positive emotions in others in AN may be related to higher levels of social anhedonia – a lack of pleasure and reward from social interaction (Tchanturia, Davies, Harrison, et al., 2012). If individuals with AN are less able to share the positive emotions of others, they may be less likely to seek out social interactions, leading to further isolation and difficulties with relationships. Further, a lack of expression of positive empathic responses during social interactions is likely to signal disinterest or rejection. This finding may be important in developing interventions that aim to increase positive emotions and develop social skills to improve social life in AN (Lyubomirsky & Layous, 2013).

In addition to intact cognitive empathy performance, the results from the MiniPONS generally do not support the hypothesis that individuals with AN have difficulties in understanding emotions and intentions through nonverbal communication. This is consistent with findings of a previous study, which did not find significant differences in performance on the TASIT in individuals with AN compared to HCs (Gramaglia et al., 2016). Considering predictors of MiniPONS performance, IQ was found to be the only significant predictor in regression models. The association between IQ and interpersonal sensitivity has been reported in several studies previously (Murphy & Hall, 2011). This might be due to some common variable involved in both understanding others and performance on IQ tests, such as attention. However the results from the regression model in this study would suggest a causal relationship – higher intelligence may allow for a better understanding of meaning from nonverbal cues. This would also explain the association found between IQ and cognitive but not affective empathy performance.

In the current study 27.5% of AN and 24% of REC met the clinical cut-off for ASD on the ADOS-2, a significantly greater proportion than in the HC group (4.3%). Past research has reported similar findings, although few studies have included a REC group (Anckarsäter et al., 2012; Bentz et al., 2017; Vagni et al., 2016; Westwood et al., 2017). It has been argued that high levels of ASD traits seen in AN are a consequence of starvation, or some other factor associated with the ill state (Hiller & Pellicano, 2013). Given that almost the same proportion of individuals in our REC group scored above the clinical cut-off, starvation is unlikely to be the major contributor to elevated ASD traits in our study. Similarly, it could be that psychomotor agitation (e.g., tapping, restlessness, fidgeting) associated with high levels of anxiety and/or depression (Zbozinek et al., 2012) in AN and REC groups is being interpreted as sensory motivated autistic behaviours on the ADOS-2. However, a recent study using the new scoring algorithm found that anxiety, depression, and BMI were not associated with ADOS-2 scores in REC or AN (Sedgewick et al., 2019). Thus, our study supports the view that ASD symptoms are stable traits in a proportion in those with AN.

8.5.1 Limitations

A limitation of the current study is the cross-sectional design. It is possible that differences in social-cognitive functioning or psychological resources contributed to the recovery of the REC group. Future research would benefit from following the same group of individuals with AN before and after recovery. Further, our study only examined a limited range of socio-emotional skills. Future studies could examine associations between comorbid psychopathology and other aspects of socio-emotional cognition in order to provide a more complete picture of the nature of social dysfunction in AN. Another limitation relates to the assessment of ASD symptoms. Although the ADOS-2 is considered a "gold-standard" tool for assessing current ASD symptoms, it does not provide enough information to give a diagnosis of ASD. Research using developmental measures in addition to assessing current symptoms would be informative in further defining social cognition in the AN+ASD subgroup. Further, the interviewer administering the ADOS-2 was not blind to the diagnostic status of the groups, potentially introducing bias into the scoring. Finally, a history of psychiatric disorders was an exclusion criteria for HCs, therefore this group may not be representative of the broader population.

8.5.2 Conclusions

Our data show that the presence of AN alone does not lead to lower empathy performance overall, with the exception of positive affective empathy. Rather, those with a previous or current diagnosis of AN plus high ASD symptoms demonstrated lower cognitive and affective empathy compared to those with low ASD symptoms. Individuals with AN and high ASD traits may require different treatment approaches or adaptations. For example, previous research has shown that patients with ASD and AN and their clinicians report difficulties in communicating with one another and a lack of understanding of each other's perspective (Kinnaird et al., 2017, 2019). While a number of interventions have been developed to target facets of social cognition in adults with ASD, improvements tend to be specific to the cognitive task in question, rather than extending to wider aspects of social life (Pallathra et al., 2019). Such

interventions might be worth exploring in individuals with AN and high ASD traits who show difficulties in empathy and emotion recognition.

8.6 References

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Chapter 9 - Discussion

The final chapter will synthesise the findings generated from each study presented in the thesis, and integrate them with relevant past literature. Clinical implications will be explored, as well as implications for understanding the aetiology and maintenance of anorexia nervosa (AN). This chapter will also outline general strengths and limitations of the thesis, and directions for future research.

9.1 Summary of thesis aims and key findings

The overall aim of the thesis was to explore the impact of comorbid autism spectrum disorder (ASD) symptoms on socio-emotional cognition in individuals in the acute and recovered stages of AN, and compare performance with healthy controls (HCs). Although high levels of depression and anxiety have long been reported in those with AN, comorbidity of ASD has only recently began to receive research attention. Such comorbidity may be particularly relevant to socio-emotional functioning, given that many of the core characteristics of ASD involve alterations in areas such as emotion recognition, social attention, and perception of nonverbal communication. The first few studies in the thesis were concerned with characterising ASD comorbidity in individuals with AN, while the latter studies explored the impact of comorbidity on socio-emotional cognition. Aims and findings from each study within the thesis are summarised below.

Study 1 – The Social Responsiveness Scale is an efficient screening tool for autism spectrum disorder traits in adults with anorexia nervosa

This study aimed to characterise ASD symptoms in individuals with AN, recovered AN (REC), and HCs using the Social Responsiveness Scale, 2nd edition (SRS-2). As well as exploring group differences, the study aimed to examine whether SRS-2 scores were associated with scores on a more comprehensive ASD assessment, the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2). Associations with eating disorder (ED) severity and functional impairment were also assessed. Individuals with AN and REC showed significantly higher SRS-2 scores than HCs, with around half of acute AN and one third of REC displaying moderate to severe difficulties in social responsiveness. SRS-2 scores were moderately positively correlated with ADOS-2

scores, and significantly predicted whether participants scored above the clinical cut-off on the ADOS-2. SRS-2 scores also positively predicted scores on the Eating Disorder Examination Questionnaire (EDE-Q) and the Work and Social Adjustment Scale (WSAS), but were not associated with body mass index (BMI).

The results suggest that ASD symptoms in individuals with AN are relatively independent of BMI, but appear to be associated with a more severe form of illness. The lack of group differences between AN and REC suggest that ASD symptoms persist after recovery, and may be an enduring trait related to AN. Finally, the study suggests that the SRS-2 may be a useful tool in identifying ASD traits in individuals with AN, and could be used for screening purposes in research or clinical settings.

Study 2 – Exploring relationships between autism spectrum disorder symptoms and eating disorder symptoms in adults with anorexia nervosa: A network approach

This study used network analysis to map relationships between ASD symptoms and ED symptoms in individuals with AN and REC, aiming to identify which symptoms from one illness were most strongly connected to symptoms of the other. Isolation, difficulties relating to others, and feelings of tension during social situations were found to be most central to the network. These symptoms had the strongest relationships with other symptoms in the network. The ASD symptom most strongly connected to ED symptoms was poor self-confidence, while the ED symptoms most strongly connected to ASD symptoms were concerns over eating around others and others seeing one's body. This study suggests social difficulties are important in maintaining psychopathology in those with AN. Further, poor self-confidence and social anxiety-type worries may partly explain why individuals with past or current AN show high scores on measures of ASD traits.

Study 3 – Self-reported autistic traits mediate reductions in social attention in adults with anorexia nervosa

This study aimed to examine group differences in attention to faces and core facial features while viewing a dynamic social scene in individuals with AN, REC, and HC. A secondary aim was to examine associations between social attention and comorbid psychopathology. Participants with AN spent less time looking at faces compared to REC and HCs, however this effect was fully mediated by self-reported ASD traits (SRS-2 scores). There were no group differences in patterns of attention to individual facial features, or time to first fixation on the face. However, a longer time to first fixation on the face was associated with higher levels of anxiety, depression, and functional impairment in individuals with AN, and higher levels of autistic traits, as measured by the ADOS-2, in HCs. The results highlight similarities in social attention in individuals with AN and women with ASD, and also suggest that the SRS-2 and ADOS-2 are differentially related to social attention in AN.

Study 4 – Emotion recognition abilities in adults with anorexia nervosa are associated with autistic traits

This study aimed to examine facial emotion recognition abilities in individuals with AN, REC, and HCs. As well as assessing group differences, relationships between emotion recognition, attention to faces, and comorbid psychopathology (ASD, social anxiety, alexithymia, depression, and anxiety) were examined. There were no significant differences across groups in emotion recognition accuracy or attention, however time spent looking at faces positively correlated with emotion recognition accuracy in the AN group only. ASD symptoms (ADOS-2 scores) predicted emotion recognition abilities, while controlling for group membership and IQ. Individuals with AN or REC who scored above the clinical cut-off on the ADOS-2 were significantly less accurate at recognising emotions than those scoring below the cut-off and HCs. The results suggest that emotion recognition difficulties are related to the presence of ASD symptoms, independent of illness state.

Study 5 – Cognitive and affective empathy in eating disorders: A systematic review and meta-analysis

Due to the mixed literature on empathic abilities in individuals with AN, study 5 aimed to provide a synthesis of studies examining empathy in those with EDs. Specifically, the review and meta-analysis examined differences in both cognitive and affective empathy in individuals with EDs, as well as associations between empathy, psychopathology, and clinical variables. Meta-analyses showed that while overall and affective empathy scores did not differ between individuals with AN and HCs, those with AN had lower cognitive empathy scores than HCs (small effect size). Only a small number of studies examined associations between empathy, ED severity, and comorbid psychopathology, however there was some evidence to suggest higher levels of alexithymia were associated with lower levels of empathy. Generally, empathy was not associated with measures of illness severity (ED psychopathology, BMI, illness duration, or general psychopathology). Similar to the profile reported in individuals with ASD, the results suggest a dissociation between affective and cognitive empathic abilities in individuals with AN.

Study 6 – Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa

This study aimed to examine group differences in empathy and perception of nonverbal communication in individuals with AN, REC, and HC, using performance-based measures. It also aimed to examine associations between socio-emotional cognition and comorbid traits (ASD, social anxiety, alexithymia, depression, and anxiety). Individuals with AN showed reduced affective empathy towards positive stimuli compared to HCs, however there were no group differences in cognitive empathy. Around one quarter of individuals with AN and REC scored above the clinical cut-off on the ADOS-2, and high ASD symptoms predicted lower cognitive and affective empathic abilities over and above the effects of group membership and demographic characteristics. Regarding perception of nonverbal communication, there was a significant group difference in perception of voice stimuli, however post-

hoc tests indicated only a trend towards poorer performance in individuals with AN compared to REC. Overall, the findings suggest only small alterations in empathic abilities and perception of nonverbal communication are associated with AN. Similar to the results of study 4, the presence of ASD symptoms in addition to a past or current diagnosis of AN seems to be associated with more difficulties in both cognitive and affective empathy.

9.2 Synthesis with existing literature

9.2.1 ASD comorbidity in AN

Findings from the cross-sectional studies presented in chapters 3, 5, 6, and 8 suggest a significantly higher proportion of those with current or past AN meet the clinical cut-off for ASD on the ADOS-2, compared to HCs. Although numbers differed slightly across studies, the highest powered study (study 6) showed that 27.5% of acute AN, 24.0% of REC, and 4.3% of HCs scored above the cut-off. These results are similar to previously published figures in adults with AN (Bentz et al., 2017; Sedgewick et al., 2019; Westwood, Mandy, & Tchanturia, 2017a). Importantly, these results suggest that around a quarter of individuals with a lifetime history of AN show high levels of ASD traits, independent of illness state. However, when examining scores quantitatively, individuals with acute AN had higher total, social affect, and restricted and repetitive interest scores compared to HCs, whereas scores in the REC group lay in the middle, not significantly different from the other two groups. This pattern of results might suggest that while some autistic symptoms are accentuated by the ill state, the ADOS-2 algorithm may be robust against picking up false positives (or false negatives in the REC group), in agreement with past research (Sedgewick et al., 2019).

In addition to the ADOS-2, the SRS-2 was used across studies in order to provide a quantitative self-report measure of ASD traits. Individuals with AN and REC demonstrated significantly higher total and subscale scores compared to HCs, with large effect sizes. The exception was the social awareness subscale, where scores in the REC group did not differ from either group, and the magnitude of the effect size for the group difference between AN and HC was also smaller. Females with ASD

demonstrate greater awareness of the need for social interaction compared to males with ASD (Lai et al., 2015), therefore this latter finding might be due to our predominantly female sample. Although this was the first investigation to use the SRS-2 in individuals with AN, mean scores were comparable to those reported in adults with ASD (Dijkhuis et al., 2019; Maddox & White, 2015; Takei et al., 2014; Walsh et al., 2019). Our results also replicated previous studies finding a positive relationship between ASD traits and functional impairment in individuals with AN (Nazar et al., 2018; Tchanturia et al., 2019).

Although study 2 was the first to explore relationships between ASD and ED symptoms using network analysis, influential nodes in the network showed similarities to those identified in previous studies. Symptoms concerning personal alienation and interpersonal sensitivity have been previously identified as core symptoms in AN psychopathology (Monteleone et al., 2019; Solmi et al., 2019), similar to the interpersonal difficulties identified in study 2. Further, the bridge symptoms that emerged from our study showed remarkable similarities to those reported by Forrest et al. (2019) in their study of trait anxiety and ED symptoms. In a sample of individuals with mixed EDs, the strongest ED bridge symptom was avoidance of social eating, whereas the strongest trait anxiety bridge node was low self-confidence. Similarly, Levinson et al. (2018) found that concerns over eating and drinking in public were the strongest bridge symptoms connecting social anxiety and ED symptoms in a mixed ED group. Social anxiety is common in individuals with AN (Kerr-Gaffney et al., 2018) as well as in ASD (Spain et al., 2018), and our findings suggest that social anxiety worries might be important in explaining comorbidity between AN and ASD. Indeed, qualitative work in women with AN and comorbid ASD has highlighted avoidance of social eating as contributing to the development of their ED. Brede et al. (2020) found that when participants initially started to restrict their food intake, they often reported skipping lunch at school in order to avoid the overwhelming social and sensory demands of the canteen environment. Thus, a number of interacting symptoms associated with ASD (social anxiety, sensory sensitivities, difficulties with social interaction) may result in avoidance of social eating, a factor which may increase risk for development of AN.

9.2.2 Socio-emotional functioning in AN

9.2.2.1 Social attention

Studies 3 and 4 provided somewhat conflicting results regarding social attention in individuals with AN. While study 4 did not find significant group differences in time spent looking at faces, individuals with AN spent significantly less time looking at faces compared to REC and HC in study 3. The differences here are likely due to differences in stimuli and task requirements. During the films expression task (FET), participants are primed to pay attention to the face stimuli in order to complete the task, and there is no other information competing for attention. On the other hand, faces in study 3 are situated within a naturalistic scene, more closely approximating a real life social encounter. Therefore, while individuals with AN may not show differences in attention during emotion recognition tasks, they may prefer to look at other parts of a scene during free viewing.

Previous studies using eye-tracking have used different measures of attention and assessed different areas of interest (AOIs), making comparisons across studies difficult. For example, Phillipou et al. (2015) found that participants with AN made a greater number of fixations of shorter duration to faces during emotion recognition compared to HCs, while Fujiwara et al. (2017) reported less time spent looking at angry and disgust faces only in individuals with AN or bulimia nervosa (BN). Similar to our findings, Dinkler et al. (2019) reported no differences in attention to faces in recovered AN compared to HCs during emotion recognition. In regards to whether attention to faces is associated with emotion recognition accuracy, our findings partially replicated those reported by Fujiwara et al. (2017), who found that lower accuracy was associated with less attention to the faces in the ED group only. In study 4, accuracy was significantly positively correlated with longer looking times to faces in the AN group only, however the association only reached trend level significance in a linear regression analysis. Only one previous study has examined attention during viewing of naturalistic scenes in AN, finding that individuals with AN spent less time looking at the eyes than HCs (Harrison et al., 2019). Individuals recovered from AN showed intermediate levels of attention; looking at the eyes significantly more than

those with AN but less than HCs. Findings from study 3 suggest that this effect may not be specific to the eyes; individuals with AN looked less at facial features overall compared to HCs and recovered AN during free viewing. Further, there were no group differences in eye to mouth viewing ratio, a finding that has been reported previously with static stimuli (Dinkler et al., 2019; Fujiwara et al., 2017).

Results of study 3 suggested that the association between group and time spent looking at faces was fully mediated by self-reported ASD traits (SRS-2 scores). That is, reduced looking times to faces in individuals with AN were due to high levels of ASD traits in this group. Only one study has previously examined the effects of ASD comorbidity on social attention, however only a recovered AN group was included. Dinkler et al. (2019) did not find any differences in attention to faces between those recovered from AN with and without comorbid ASD. In contrast, our study demonstrated that ASD traits explain significant variation in social attention in a large sample of acute and recovered AN. Importantly, this effect was only found for self-reported ASD traits measured by the SRS-2, and not ADOS-2 scores. Although results from study 1 suggested moderate correlations between the two measures, study 3 suggests important differences in the extent to which ASD measures may relate to real-life social behaviour. That scores on the ADOS-2 predicted empathy and emotion recognition abilities but not social attention suggests it may be more closely related to higher-order social cognitive abilities involving social understanding and mentalising. On the other hand, the SRS-2 may be related to more automatic, responsive social processes, such as attention. Indeed, associations between reduced attention to faces and higher SRS-2 scores have previously been found in adults with ASD (Dijkhuis et al., 2019; Ketelaars et al., 2017).

Although higher levels of alexithymia were also significantly correlated with reduced looking times to faces, TAS-20 scores did not significantly predict looking times in hierarchical regression analyses. Thus, although both ASD traits and alexithymia were associated with social attention, it seems that the effects of ASD traits subsume those of alexithymia. This result is in agreement with Fujiwara et al. (2017), who suggested alexithymia may have a modest role in social attention in individuals with EDs.

9.2.2.2 Perception of nonverbal communication

Generally, results from studies 4 and 6 suggest that individuals with AN do not show difficulties in understanding nonverbal communication, either through facial expressions, body movements and gestures, or through tone of voice. Our findings contrast with previous studies reporting difficulties in both basic and complex facial emotion recognition in individuals with AN (Oldershaw et al., 2011). Past research examining perception of nonverbal communication through other channels has also found subtle differences in individuals with past or current AN. For example, Bentz et al. (2017) found that individuals recovered from AN were significantly poorer at understanding body and voice information compared to individuals with AN and HCs. In contrast, although our study found a significant group difference in perception of voice stimuli, post-hoc tests indicated a trend towards significantly lower performance in the AN group compared to REC. Studies using other paradigms, such as the reading the mind in the voice task, have also found significantly lower performance in AN compared to HCs (Kucharska-Pietura et al., 2004; Oldershaw et al., 2010). Given that our sample size was larger than that of previous studies, it is unlikely that our study was too underpowered to detect group differences. It is also unlikely that participants in our study had a less severe illness than previous study samples, and therefore presented with fewer difficulties. Although only a minority of participants were receiving inpatient treatment at the time of testing, mean illness duration was over seven years, representing a severe and enduring illness.

Results from study 4 suggest that difficulties in facial emotion recognition abilities may only be present in a sub-sample of individuals with AN and high ASD traits. It is therefore possible that variations in ASD symptoms across study samples have contributed to the mixed findings regarding emotion recognition and other domains of nonverbal communication in AN. Thus far, few studies have examined the impact of ASD symptoms on perception of nonverbal communication in AN. Dinkler et al (2019) examined facial emotion recognition abilities in women recovered from AN, comparing those with and without comorbid ASD. In contrast to our findings, those with ASD were more accurate at identifying emotions than those without ASD. The mixed findings may be due to differences in samples; participants in the previous

study were older and represented a long-term recovered group (80% had been recovered for at least 12 years), and a diagnosis of ASD was confirmed over a number of assessments. Further, given the very small sample size of the comorbid ASD group (*n* = 6), results should be interpreted with caution. Although high levels of ASD symptoms were significantly correlated with poorer performance on both the Mini Profile of Nonverbal Sensitivity (MiniPONS) (study 6) and the FET (study 4), hierarchical regression analyses showed that ASD symptoms explained significant variance in performance on the FET only. It could be the case that performance on the MiniPONS is influenced more by intelligence than was our facial emotion recognition paradigm. Indeed, IQ was the only significant predictor of MiniPONS performance, and previous research has shown robust associations between task performance and IQ (Murphy & Hall, 2011).

9.2.2.3 Empathy

Findings from studies 5 and 6 provided somewhat conflicting results. While results of the meta-analysis suggested that individuals with AN showed lower levels of self-reported cognitive empathy compared to HCs, study 6 did not find differences in actual cognitive empathy performance. Instead, individuals with AN showed lowered affective empathy towards positive stimuli only, with a medium effect size. It may be that the differing results are due to the use of self-report versus performance-based measures of empathy. Discrepancies between self-report and performance-based measures have been demonstrated in other psychiatric populations, such as schizophrenia (Bonfils et al., 2016; Derntl et al., 2009). It is likely that the two studies measured slightly different constructs; while the review measured individuals' perceptions of their own empathic abilities, our empirical investigation using the multifaceted empathy test (MET) measured actual empathic responses. Reporting on one's own emotional responses may be particularly difficult for those with high levels of alexithymia, as was the case in our AN group. Study 6 therefore addresses some of the limitations of self-report measures, which might be particularly pertinent to individuals with AN.

However, our results also differ from the few studies that have previously used performance-based measures of empathy, which have not found group differences in affective empathy in participants with AN or BN compared to HCs (Brewer et al., 2019; Cardi, Corfield, et al., 2015). The use of different tasks and inclusion of mixed ED groups are likely to explain the mixed results. Generally, difficulties in socio-emotional functioning tend to be somewhat less prominent in individuals with BN compared to AN (Bora & Kose, 2016). Further, past studies did not assess positive and negative affective empathy, as in our study. Our results suggest this distinction is important in individuals with AN. Despite the differences with previous empathy research, our results are consistent with past work examining related concepts. For example, whilst individuals with AN show similar facial expressivity to HCs while viewing negatively valanced stimuli, they display fewer positive facial expressions in response to positive stimuli (Cardi, Corfield, et al., 2014; Lang, Larsson, et al., 2016; Leppanen, Dapelo, et al., 2017). Difficulties in sharing positive affect with others may also be related to high levels of social anhedonia reported in those with AN (Tchanturia, Davies, Harrison, et al., 2012). Taken together, these results may indicate wider dysfunction in positive affective processes in individuals with AN.

Until now, few studies have examined the impact of comorbid psychopathology on empathic abilities in individuals with AN. One study demonstrated that high levels of alexithymia were associated with lower levels of self-reported empathy in AN (Adenzato et al., 2012), while another found that increased affective empathy (specifically in response to others' pain) was associated with higher alexithymia (Brewer et al., 2019). Our study replicated findings from the former study, finding significant negative correlations between alexithymia and cognitive and affective empathy. However, hierarchical regression analyses did not suggest alexithymia was an important predictor of empathic abilities. Instead, only ASD symptoms predicted both cognitive and affective empathic abilities whilst controlling for associated demographic characteristics and group membership. To our knowledge, this is the first study to examine the relationship between empathic abilities and ASD traits in individuals with AN. However, a similar pattern of results has been reported in a related domain, theory of mind (ToM). Anckarsäter et al. (2012) found that those

with AN and comorbid ASD showed significant difficulties in identifying mental states in others compared to HCs, whereas those with AN only did not show any difficulties. In sum, these results suggest that difficulties in both cognitive and affective empathy are associated with ASD traits, rather than the ED per se.

9.2.2.4 Similarities and differences with other psychiatric disorders

The results of the current thesis suggest a number of similarities and differences in social cognition between AN and other psychiatric disorders. Traditionally, psychiatric disorders have been conceptualised as distinct entities based on sets of observable symptoms. However, this approach has led to several problems, including high levels of comorbidity and presentations that do not fit into diagnostic categories (Cuthbert & Insel, 2010). Consequently, there has been a move towards characterising psychopathology in terms of a continuum of functioning on various dimensions of behaviour and neurobiological measures (e.g., cognitive, social). By highlighting similarities between AN and other psychiatric disorders, hypotheses regarding shared risk factors or disease processes may be generated.

Results from study 5 suggested that individuals with AN may show a similar empathic profile to those with ASD, characterised by lower cognitive empathy and intact affective empathy (Dziobek et al., 2008). However, results from study 6 revealed that actual empathic abilities did not show this pattern. Instead, a moderate reduction in positive affective empathy only seems to be a finding unique to AN. While difficulties in affective empathy have also been found in individuals with schizophrenia, this effect has been found to be more general; affecting both positive and negative affective empathy in addition to cognitive empathy (Bonfils et al., 2016; Derntl et al., 2009). Similarly, increases in affective empathy are associated with the manic state in those with bipolar disorder (Bodnar & Rybakowski, 2017), in the opposite direction to our observations in AN. That reduced positive affective empathy was found in the acute state of AN only suggests this may be a state rather than trait effect. Several partially separable brain pathways (all requiring the superior temporal cortex) are hypothesised to be involved in affective empathy, depending on the valence of the emotion the individual is responding to (Blair, 2005). The amygdala is involved in

processing of happiness, however both increased and decreased activity has been reported (Breiter et al., 1996; Morris et al., 1996). Neuroimaging evidence suggests both structural and functional alterations in the amygdala in AN (Joos et al., 2011; Leppanen, Cardi, et al., 2017), suggesting a possible link between brain function and altered positive affective empathy. Future studies measuring amygdala activity during empathic responding in individuals with AN may provide insight into the underlying mechanisms responsible for our behavioural results.

In contrast, our results suggest similar processes may underlie social attention in individuals with AN and other disorders. Reduced attention to faces has been well documented in individuals with ASD (Frazier et al., 2017) and social anxiety disorder (SAD; Chen & Clarke, 2017). Given the mediating effects of ASD traits found in study 3, theories relating to altered social attention in individuals with ASD may be particularly relevant. Neuroimaging studies have suggested that attention to faces in individuals with ASD is associated with increased amygdala activation, possibly reflecting heightened sensitivity to social stimuli (Dalton et al., 2005). As a result, individuals with ASD may avoid attending to faces and eyes in an attempt to reduce hyperarousal. Indeed, individuals with AN show high levels of social anxiety, as well as higher sensitivity to social exclusion compared to HCs (Cardi, Tchanturia, et al., 2018; Kerr-Gaffney et al., 2018; Meneguzzo et al., 2020). Therefore, it may be the case that individuals with AN also find attending to social stimuli or engaging in social interactions uncomfortable, resulting in avoidance and reduced social attention.

Alternatively, reductions in social attention in AN may be a result of reduced social motivation, a mechanism proposed to underly similar findings in those with ASD (Chevallier et al., 2012). Social motivation encompasses a variety of dispositions that bias humans to attend to social stimuli, build social bonds, and seek and take pleasure from social interactions. By this account, difficulties in social cognition are a consequence, rather than cause of reduced social motivation. Although research into social motivation in AN is lacking, there is some evidence to suggest differences in this domain. For example, individuals with AN show high levels of social anhedonia, a symptom that persists after recovery (Harrison et al., 2014). Along with reduced attention to faces, Watson et al. (2010) found that in a monetary choice task,

individuals with AN did not sacrifice money to see faces as HCs did, suggesting differences in social reward processing. Differences in activity in the reward circuitry in response to food and monetary rewards have also been documented in individuals with AN, suggesting a more general deficit in reward processing (Keating et al., 2012; Uher et al., 2004; Wagner et al., 2007).

9.3 Clinical implications and future directions

Generally, results from studies 3, 4, 5, and 6 suggest only small alterations in some domains of socio-emotional cognition in individuals with AN. While individuals with AN demonstrated lower empathic abilities and reduced social attention compared to REC and HCs, no group differences in facial emotion recognition and perception of nonverbal communication were found. Our results therefore provide partial support for maintenance models of AN, which emphasise differences in socio-emotional cognition as key factors in the development and maintenance of the illness (Treasure & Schmidt, 2013). Our results do support the notion that underlying differences in social cognition may be related to interpersonal difficulties associated with AN. For example, difficulties in affective empathy and delayed fixation to faces were significantly associated with functional impairment in individuals with AN, as measured by the WSAS. A lack of expression of positive empathic responses, paired with reduced attention to faces may signal disinterest or rejection during social interactions. This may make it difficult to build and maintain relationships, leading to isolation and reduced social networks. Indeed, findings from our network analysis highlighted isolation and interpersonal difficulties as central to maintaining psychopathology in our sample. Central symptoms are hypothesised to have prognostic utility; reducing these symptoms should result in reductions in other symptoms in the network (Elliott et al., 2019; McNally, 2016). Given that social relationships have been identified as an important factor in recovery from AN (Federici & Kaplan, 2008; Linville et al., 2012), treatments that attempt to improve aspects of socio-emotional cognition and associated interpersonal difficulties may be beneficial.

Despite subtle group differences in empathy and social attention, results from studies 3, 4, and 6 suggested that ASD traits were overall better predictors of socio-emotional cognition than AN status. Thus far, much of AN and ASD comorbidity research has focussed on group differences on clinical measures of ASD symptoms, such as the autism quotient (AQ) or the ADOS-2 (e.g., Dell'Osso et al., 2018; Gillberg & Råstam, 1992; Mandy & Tchanturia, 2015; Rhind et al., 2014; Sedgewick et al., 2019; Tchanturia et al., 2019; Westwood et al., 2018). Generally, these studies have shown higher rates of ASD symptoms in individuals with AN compared to HCs, perhaps also including associations with other psychiatric symptoms, such as ED psychopathology. In contrast, our investigation characterised the socio-emotional profile associated with high ASD traits in individuals with a lifetime history of AN, showing that high levels of ASD traits are associated with lower empathy and facial emotion recognition performance, as well as reduced social attention. Differences in these domains have repeatedly been demonstrated in individuals with ASD (Chita-Tegmark, 2016; Frazier et al., 2017; Kok et al., 2016; Loth et al., 2018; Peñuelas-Calvo et al., 2019). Although we did not confirm diagnoses of ASD in the current investigation, our results support the notion that a significant proportion of individuals with AN may also have ASD, accompanied by similar alterations in socio-emotional cognition.

These results have important implications for our understanding of the aetiology and maintenance of AN, as well as implications for treatment. Firstly, our results suggest that distinct subgroups within the overall diagnosis of AN may exist, potentially with different developmental pathways. Given that ASD is a neurodevelopmental disorder with symptoms presenting from early childhood, it may be the case that certain characteristics of ASD contribute to the development of AN in those with both disorders. For example, women with ASD in particular show sensory sensitivities to the taste, texture, and smell of food, resulting in a limited range of acceptable foods (Sharp et al., 2013; Spek et al., 2019). Energy deficits may arise as a result of such food restriction, a potential trigger for the development of AN (Madra & Zeltser, 2016). Similarly, rigid thinking styles and intense interests associated with ASD may precipitate the development of AN. Those with AN and high ASD traits show higher levels of cognitive rigidity and set-shifting difficulties than those with low ASD

symptoms (Westwood, Mandy, & Tchanturia, 2017b), and women with AN and ASD have described intense interests in topics such as exercise and nutrition often contributing to the development of their AN (Brede et al., 2020). ASD symptoms, including differences in socio-emotional cognition identified in our investigation, may also contribute to the development of AN in more indirect ways. Difficulties in social interaction and understanding may result in bullying and negative social experiences with peers, especially during adolescence (Tierney et al., 2016). Restricting food intake may be a means of numbing the resulting emotional distress and anxiety (Brede et al., 2020).

Those with AN and high ASD traits may require adaptations to treatment. This is a gap identified in qualitative studies, which have found that individuals with AN and ASD and their clinicians report difficulties in communicating with one another and a lack of understanding of each other's perspective (Kinnaird et al., 2017, 2019). Patients also reported that their autistic traits made it difficult to engage in treatment, which was often misinterpreted by clinicians. For example, being unable to eat during meal times could be due to sensory sensitivities (e.g., being unable to eat certain foods due to the texture, or noise in inpatient dining rooms), however this was often attributed to stubbornness or more typical ED worries over the nutritional content of food (Kinnaird et al., 2019). Participants believed that a more individualised treatment approach would be beneficial, working collaboratively with clinicians to make adjustments to accommodate their ASD symptoms. Relevant to the current thesis, these adaptations may include work on identifying and communicating emotions, and alternative methods of communication (e.g., writing things down to bring to therapy sessions or appointments). In addition, clinicians should have an understanding of ASD and its implications for ED treatment. For example, lowered social attention in those with AN could be misinterpreted as disinterest during interactions with clinicians, when it is in fact a symptom associated with ASD. Similarly, patients may find it difficult to empathise with their clinician's point of view when making treatment decisions. This could be misinterpreted as stubbornness or unwillingness to make changes towards recovery, but again may

reflect underlying symptoms associated with ASD. Thus, providing training on ASD for clinicians working with patients with AN may be important in improving treatment.

Based on the results of our investigation, the type of treatment offered to individuals with AN and high ASD traits may also require consideration. Although we found differences in several domains of social cognition, attempts to "treat" such differences should be approached with some caution. ASD is a neurodevelopmental disorder present from birth, symptoms of which are thought to be a result of structural and functional differences in the brain (Ecker et al., 2015). As a result, the aim of psychotherapy or other treatments for individuals with ASD is not to change these differences, but to help them deal and adapt to the world around them, increase positive coping strategies and behaviours, and improve mental health. Our results suggest that interventions such as social or emotional skills training may be useful in those with AN and high ASD traits. Social skills training has been shown to be beneficial in improving social cognition, social skills knowledge, and friendship quality in individuals with ASD (Hillier et al., 2007; Kandalaft et al., 2013; Turner-Brown et al., 2008). There is also evidence to suggest that such interventions also improve levels of anxiety and depression, outcomes which may be important in improving quality of life in those with AN (Hillier et al., 2011; Yoo et al., 2014).

A few interventions for AN have incorporated aspects of emotion and social skills training, such as Cognitive Remediation and Emotion Skills Training (CREST; Davies et al., 2012). CREST includes modules on identifying and communicating one's own emotions, as well as identifying emotions in others, and has been shown to improve social anhedonia and alexithymia in individuals with AN (Tchanturia et al., 2014, 2015). Targeting emotion recognition specifically, a recent study showed that patients with AN who received a computerised social cognition training session showed greater improvements in emotion recognition abilities and ED symptoms compared to those who received sham training (Preis et al., 2020). Assessing whether treatments such as CREST and social skills training are useful for those with AN and ASD is an important question for future research. This issue is especially pressing given that the presence of high ASD traits in AN is associated with poorer treatment

outcomes and the need for more intensive treatments (Nazar et al., 2018; Stewart et al., 2017; Tchanturia et al., 2016).

9.4 Thesis limitations

A number of limitations should be noted. Firstly, we were unable to confirm a diagnosis of ASD, or indeed other comorbid psychiatric disorders in our sample. Although the ADOS-2 is recommended as part of an ASD diagnostic assessment (National Institute for Health and Care Excellence [NICE], 2012), it does not provide enough information alone to give a diagnosis of ASD. As well as an assessment of current symptoms, diagnostic assessments should also include developmental histories and information on behavioural problems, sensory sensitivities, and functioning at home, in education, or employment. An assessment of early developmental history would be particularly useful in the current study, as this would confirm whether symptoms of ASD were present before the onset of AN. Given that our recovered group showed similar levels of ASD symptoms to acute AN, it is unlikely that ASD symptoms are a result of starvation or low BMI. However, it could be that high levels of general psychopathology in both the acute and recovered AN groups resulted in elevated scores on ASD measures. Although past research has shown that scores on the ADOS-2 are not related to anxiety and depression in AN (Sedgewick et al., 2019), an assessment of ASD symptoms in childhood would help clarify longitudinal relationships between symptoms and potential aetiological pathways.

A somewhat related issue concerns our study sample and design. Cross-sectional investigations assessing group differences between acute and recovered individuals are limited, as potential confounds are introduced. That is, it is possible that some difference in psychopathology or other psychological factor contributed to the recovery of our recovered AN group, which may have influenced our findings. Although illness duration did not differ across groups, the recovered AN group were diagnosed significantly earlier than the acute AN group, a factor which could signal different processes in illness development. Longitudinal studies would provide additional insight into relationships between socio-emotional cognition and ASD traits before and after recovery. Similarly, only adults were included in our

investigation. Much less research has investigated socio-emotional cognition in adolescents with AN, however there is some evidence to suggest more severe difficulties in domains such as emotion recognition (Lang et al., 2015). Future studies would benefit from including a sample of adolescents with AN, in order to better understand developmental processes underpinning socio-emotional abilities.

Although significant differences were found in socio-emotional cognition in those with AN and high ASD traits (AN+ASD) compared to those with low ASD traits and HCs, it is not known whether these differences are of similar magnitude to those observed in individuals with a diagnosis of ASD only. Our investigation would therefore have benefited from the inclusion of an ASD group, in order to understand whether similar processes may underlie social cognition in ASD and AN+ASD. If performance on socio-cognitive tasks was similar across AN+ASD and ASD groups, this would provide additional evidence supporting "true" ASD comorbidity in AN. Very few studies have investigated this issue, and those that have have had various methodological problems. A meta-analysis investigating ToM abilities in individuals with AN and individuals with ASD compared to HCs found that generally, effect sizes were greater in ASD than in AN, which could suggest differences in social understanding between the two disorders (Leppanen et al., 2018). However, most ASD studies included majority male samples, and AN studies majority female samples. Further, gender emerged as a moderator explaining significant heterogeneity between studies. Since male gender is associated with lower socio-cognitive abilities in the general population (Adenzato et al., 2017; Wacker et al., 2017), it is plausible the larger effect sizes seen in ASD compared to AN are in part due to gender differences across samples. It is possible that females with ASD would show similar socio-cognitive profiles to females with AN. Building on the current investigation, future research would benefit from examining empathy, perception of nonverbal communication, and social attention in those with AN compared to ASD, matching groups for sex. Such research would be particularly relevant given recent interest in understanding the female ASD phenotype (Harrop et al., 2018; Lai et al., 2011, 2015).

It must also be noted that although ASD symptoms predicted empathy, emotion recognition, and social attention, results somewhat differed depending on the measure of ASD symptoms used. Further studies in individuals with AN and a clinician-confirmed diagnosis on ASD may help clarify whether the SRS-2, and indeed the ADOS-2, are reliable and valid measures of ASD symptoms in individuals with AN. Finally, in the regression models presented in studies 3, 4, and 6, the proportion of variance in socio-emotional abilities explained by ASD symptoms was relatively small. It is likely that other unmeasured characteristics also contribute to socio-emotional abilities in individuals with AN.

9.5 Thesis strengths

A particular strength of the current investigation relates to the novel methods employed. For example, our study was the first to use the SRS-2 in individuals with AN. Given the growing interest in ASD comorbidity in individuals with AN, an important issue for both clinicians and researchers relates to how ASD symptoms should be assessed. Study 1 provided important information regarding the utility of the SRS-2, a measure that has been used extensively in ASD research. Similarly, study 2 was the first study to examine associations between ED and ASD traits in individuals with AN using network analysis. Network analysis provides a way of identifying which symptoms of AN may be involved in the development of other comorbid disorders. Such a method may be particularly useful in those with AN, considering the very high rates of comorbidity in this population (Hudson et al., 2007; Ulfvebrand et al., 2015). To assess domains of socio-emotional cognition, the current investigation used various paradigms that have not yet been used extensively in those with AN, but have been used in other psychiatric disorders. This was intended to encourage comparisons between AN and other disorders, and potentially highlight transdiagnostic mechanisms underlying difficulties in socio-emotional cognition. For example, only one study has previously used eye-tracking to capture social attention to naturalistic, dynamic stimuli in AN, and only investigated attention to eyes (Harrison et al., 2019). Study 3 was therefore the first to measure attention to the core facial features using dynamic stimuli in individuals with AN, using similar stimuli

and analytic methods to those used in ASD research (Dijkhuis et al., 2019; Ketelaars et al., 2017; Klin et al., 2002; Rice et al., 2012). Similarly, study 6 was the first to use a performance-based measure of cognitive and affective empathy in individuals with AN, highlighting differences from past research using self-report measures.

Another strength is our sample size. In our systematic review of eye-tracking research in EDs, small sample size was identified as a limitation of past research. Studies 3 and 4 are the largest studies to date examining social attention using eye-tracking in individuals with AN. Other strengths related to the representativeness of our sample. Both males and females were included, as well as inpatients, outpatients, and those who were not currently receiving treatment. Although as many as 25% of those with EDs are male, males continue to be excluded from ED research due to their perceived atypicality (Murray et al., 2018). Similarly, by including individuals with AN who were not currently seeking treatment, it was hoped that a more diverse range of presentations would be included. On the other hand, this method of recruitment may have introduced a self-selection bias. Given that participants with AN were not recruited through consecutive referrals to ED services, there may have been differences between those that chose to take part in our research and those who did not.

9.6 Conclusion

To conclude, the findings from this thesis provide novel insights into the relationship between socio-emotional functioning and ASD symptoms in individuals with AN. The first few studies focussed on the measurement of ASD symptoms and their associations with ED symptoms. Results from study 1 confirmed the presence of high levels of ASD symptoms in individuals in the acute and recovered stages of AN, on both questionnaire and clinical interview measures. Study 2 found that that poor self-confidence and social anxiety-type worries mediated the relationship between ASD and ED symptoms in acute and recovered AN. In subsequent studies, differences in empathic abilities, perception of nonverbal communication, and social attention were explored across AN, recovered AN, and HCs. Generally, only small differences in socio-emotional cognition were found in those with AN. Overall, ASD symptoms

were better predictors of socio-emotional abilities than ED status: high levels of ASD symptoms predicted lower cognitive and affective empathic abilities, emotion recognition performance, and attention to faces, while controlling for group membership.

These findings highlight the importance of clinical heterogeneity within the overall diagnosis of AN, and suggest that AN with and without high ASD traits may represent two qualitatively different conditions. Importantly, the findings suggest that not all individuals with AN experience difficulties in socio-emotional cognition. Differences in socio-emotional cognition may suggest different aetiological pathways and maintenance factors, and may moderate responses to treatment. Future research should more precisely characterise these differences by including a sub-sample of individuals with a confirmed diagnosis of ASD in addition to AN. Research may also benefit from directly comparing those with ASD to those with AN, in order to help elucidate similarities and differences in the underlying processes responsible for difficulties in socio-emotional cognition.

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Appendices

Appendix A. Supplementary material for published review in introduction

Supplementary table 1. Risk of bias assessment, based on the Kmet form for quantitative analysis

Study	A	B	C	D	E	F	G	H	I	J	K	Total	%
Baldofski et al. (2018)	2	2	1	2	2	1	2	2	2	2	2	20	91
Bauer, Schneider, Waldorf, Braks et al. (2017)	2	2	2	2	2	1	2	2	1	2	2	20	91
Bauer, Schneider, Waldorf, Cordes et al. (2017)	2	2	2	2	2	1	2	2	0	2	2	19	86
Blechert et al. (2009)	2	2	2	2	2	1	2	1	2	2	2	20	91
Blechert et al. (2010)	2	1	2	2	2	0	2	1	1	2	2	17	77
Cornelissen et al. (2016)	2	2	1	2	2	2	2	2	1	2	2	20	91
Freeman et al. (1991)	2	1	1	2	1	0	0	2	0	2	2	13	59
Fujiwara et al. (2017)	2	2	1	1	2	1	2	2	2	2	2	19	86
George et al. (2011)	2	2	2	2	2	0	2	2	0	2	2	18	82
Giel et al. (2011)	2	2	1	1	2	0	2	2	2	2	2	18	82

Giel et al. (2013)	2	2	2	2	2	0	2	1	2	2	2	19	86
Godier et al. (2016)	2	1	2	2	1	0	1	1	1	2	2	15	68
Horndasch et al. (2012)	1	2	1	2	2	0	2	2	0	2	2	16	73
Kollei et al. (2017)	2	1	2	2	2	1	2	2	2	2	2	20	91
Leehr et al. (2016)	2	2	1	2	2	1	2	2	1	2	2	19	86
Leehr et al. (2018)	2	2	2	2	2	1	2	2	1	2	2	20	91
Pallanti et al. (1998)	2	2	2	1	2	1	2	2	1	1	2	18	82
Phillipou et al. (2014)	2	2	2	2	2	1	1	2	0	2	2	18	82
Phillipou et al. (2015)	2	2	2	2	2	1	2	2	1	2	2	20	91
Phillipou, Rossell, Gurvich, Castle et al. (2016)	2	2	2	2	2	1	2	2	1	2	2	20	91
Phillipou, Rossell, Gurvich, Highes et al. (2016)	2	2	2	2	2	1	2	2	0	2	2	19	86
Pinhas et al. (2014)	2	2	2	1	2	0	2	2	0	2	2	17	77
Schag et al. (2013)	2	2	1	2	2	1	2	2	2	2	2	20	91
Schmidt et al. (2016)	2	2	2	2	2	1	2	2	2	2	2	21	95

Sperling et al. (2017)	2	2	1	2	2	2	2	2	2	2	2	21	95
Svaldi et al. (2011)	2	2	1	1	2	0	1	0	1	1	2	13	59
Svaldi et al. (2012)	2	1	2	1	2	1	1	0	1	1	2	14	64
Svaldi et al. (2016)	2	1	2	2	2	0	2	0	1	1	2	15	68
Tuschen-Caffier et al. (2015)	2	1	2	2	2	0	2	0	1	1	2	15	68
Von Wietersheim et al. (2012)	2	2	2	2	2	1	2	2	1	2	2	20	91
Watson et al. (2010)	2	1	2	0	2	0	2	1	1	1	2	14	64

A, Question/objective sufficiently described? B, Study design evident & appropriate? C, Method of subject/comparison group selection described and appropriate? D, Subject and comparison group characteristics described? E, Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias? F, Sample size appropriate? G, Analytic methods described/justified and appropriate? H, Some estimate of variance is reported for the main results? I, Controlled for confounding variables? J, Results reported in sufficient detail? K, Conclusions supported by the results?

Supplementary table 2. Outcome measures used across studies

Outcome measure	Description
Gaze direction bias/initial fixation position	Number of first fixations on stimuli of interest as a proportion of all first fixations
Gaze duration bias	Mean time spent looking at stimuli A minus mean time spent looking at stimuli B.
Detection bias score	Mean reaction time on non-target trials minus mean reaction time on target trials
Fixation/dwell times	Overall looking times at areas of interest
Saccade latency	Time between stimulus presentation and first saccade
Saccade difference score	Saccade latency for stimulus A trials minus saccade latency for stimulus B trials
Fixation count/gaze frequency	Number of fixations in a given area of interest
Evaluative gaze index	Evaluative rating of each body part multiplied by the fraction of time spent looking at that area. This figure is then summed across all body areas. Higher scores indicate more time spent looking at positively rated areas.

Eye-preference	Time spent looking at eyes minus time spent looking at mouths (proportional to time spent looking at faces)
Saccade rate	Frequency of saccades within an area of interest
Initial fixation duration bias	Mean duration of initial fixations on stimulus A minus duration of initial fixations on stimulus B.
Gaze latency bias	Time between trial onset and first fixation on stimulus A minus that of stimulus B.
X-span and Y-span	Movement from central position on the X-axis and Y-axis respectively
P-span	Change in pupil size
Number of first saccade errors	Number of first saccades made in the direction of the stimulus in an antisaccade task
Number of second saccade errors	Number of second saccades made in the direction of the stimulus in an antisaccade task
Typical target velocity	The rate at which smooth pursuit percent gain decreases as target velocity increases; a measure of change in peak performance

Typical matching target velocity	Change in global performance during smooth pursuit
Anticipatory saccades	Anticipatory jumps ahead of the target during smooth pursuit
Square wave jerk (SWJ) rate	Number of SWJs, a type of saccadic intrusion during fixation
Fixation duration	Mean duration of fixations
Saccade amplitude	Mean size of saccades
Feature fixation index	Number of fixations to salient minus non-salient features, divided by total fixations
Feature duration index	Duration of fixations to salient minus non-salient features, divided by total duration
Gain	Ratio between primary saccade and target amplitude
Intersaccadic interval	Interval between saccade onsets
Peak velocity	Highest velocity reached during saccades
Inhibitory error rate	Frequency of saccades towards the stimulus before the response period

Directional error rate	Frequency of saccades in the wrong direction
PAN error rate	Frequency of incorrect saccades in prosaccade, antisaccade, and no-go tasks
Sequential errors	Proportion of errors on both the first and second saccade; i.e., when participants failed to correct errors
1st fixation direction	Frequency of first fixations directed to a stimulus
1st fixation duration	Duration of first fixation
2nd fixation direction	Frequency of second fixations directed to a stimulus
2nd fixation duration	Duration of second fixation

Appendix B. Self-report questionnaires

EDE-Q

The following questions are concerned with the past four weeks only (28 days). Please read each question carefully and tick the appropriate box.

Please answer all the questions.

On how many of the past 28 days…	No days	1-5 days	6-12 days	13-15 days	16-22 days	23-27 days	Every day
1. Have you been deliberately trying to limit the amount of food you eat to influence your shape or weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
2. Have you gone for long periods of time (8 waking hours or more) without eating anything at all in order to influence your shape or weight?	0	1	2	3	4	5	6
3. Have you tried to exclude from your diet any foods that you like in order to influence your shape or weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
4. Have you tried to follow definite rules regarding your eating (for example, a calorie limit) in order to influence your shape or weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
5. Have you had a definite desire to have any empty stomach with the aim of	0	1	2	3	4	5	6

influencing your shape or weight?							
6. Have you had a definite desire to have a totally flat stomach?	0	1	2	3	4	5	6
7. Has thinking about food, eating, or calories made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?	0	1	2	3	4	5	6
8. Has thinking about shape or weight made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?	0	1	2	3	4	5	6
9. Have you had a definite fear of losing control over eating?	0	1	2	3	4	5	6
10. Have you had a definite fear that you might gain weight?	0	1	2	3	4	5	6
11. Have you felt fat?	0	1	2	3	4	5	6
12. Have you had a strong desire to lose weight?	0	1	2	3	4	5	6

Questions 13-18: Please fill in the appropriate number in the boxes on the right. Remember that the questions only refer to the past four weeks (28 days).

13. Over the past 28 days, how many times have you eaten what other people would regard as an unusually large amount of food (given the circumstances)? _____

14. …On how many of these times did you have a sense of having lost control over your eating (at the time that you were eating)? _____

15. Over the past 28 days, how many DAYS have such episodes of overeating occurred (i.e., you have eaten an unusually large amount of food and have had a sense of loss of control at the time)? _____

16. Over the past 28 days, how many times have you made yourself sick (vomit) as a means of controlling your shape or weight? _____

17. Over the past 28 days, how many times have you taken laxatives as a means of controlling your shape or weight? _____

18. Over the past 28 days, how many times have you exercised in a "driven" or "compulsive" way as a means of controlling your weight, shape, or amount of fat, or to burn off calories?

_____

Questions 19 to 20: please circle the appropriate number. Please note that the term "binge eating" means eating what others would regard as an unusually large amount of food for the circumstances, accompanied by a sense of having lost control over eating.

On how many of the past 28 days…	No days	1-5 days	6-12 days	13-15 days	16-22 days	23-27 days	Every day
19. How many days have you eaten in secret? Do not count episodes of binge eating.	0	1	2	3	4	5	6

	None of the time	A few of the times	Less than half	Half of the times	More than half	Most of the time	Every time
20. On what proportion of the times that you have eaten have you felt guilty because of its effect on your shape or weight? Do not count episodes of binge eating.	0	1	2	3	4	5	6

Questions 21 to 28: Please circle the appropriate number on the right. Remember that the questions only refer to the past four weeks (28 days).

Over the past 28 days…	Not at all		Slightly		Moderately		Markedly
21. How concerned have you been about other people seeing you eat? Do not count episodes of binge eating.	0	1	2	3	4	5	6
22. Has your weight influenced how you think about (judge) yourself as a person?	0	1	2	3	4	5	6
23. Has your shape influenced how you think about (judge) yourself as a person?	0	1	2	3	4	5	6
24. How much would it have upset you if you had been asked to weigh yourself once a week (no more, or less, often) for the next four weeks?	0	1	2	3	4	5	6
25. How dissatisfied have you been with your weight?	0	1	2	3	4	5	6
26. How dissatisfied have you been with your shape?	0	1	2	3	4	5	6
27. How uncomfortable have you felt seeing your body (for example, seeing your shape in the mirror, in a shop window reflection, while undressing or taking a bath or shower)?	0	1	2	3	4	5	6
28. How uncomfortable have you felt about others seeing your shape or figure (for example, in communal changing rooms, when	0	1	2	3	4	5	6

swimming, or wearing tight clothes?							

HADS

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings, he or she will be able to help you more. This questionnaire is designed to help your clinician to know how you feel. Read each item below circle the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long, thought out response.

A	D			A	D
		I feel tense or 'wound up'	**I feel as if I am slowed down**		
3		Most of the time	Nearly all of the time		3
2		A lot of the time	Very often		2
1		From time to time, occasionally	Sometimes		1
0		Not at all	Not at all		0
		I still enjoy the things I used to enjoy	**I get a sort of frightened feeling like butterflies in the stomach**		
	0	Definitely as much	Not at all	0	
	1	Not quite as much	Occasionally	1	
	2	Only a little	Quite often	2	
	3	Hardly at all	Very often	3	
		I get a sort of frightened feeling as if something awful is about to happen	**I have lost interest in my appearance**		
3		Very definitely and quite badly	Definitely		3
2		Yes, but not too badly	I don't take as much care as I should		2
1		A little, but it doesn't worry me	I may not take quite as much care		1
0		Not at all	I take just as much care as ever		0
		I can laugh and see the funny side of things	**I feel restless as if I have to be on the move**		
	0	As much as I could	Very much indeed	3	
	1	Not quite so much now	Quite a lot	2	
	2	Definitely not so much now	Not very much	1	
	3	Not at all	Not at all	0	
		Worrying thoughts go through my mind	**I look forward with enjoyment to things**		
3		A great deal of time	As much as I ever did		0
2		A lot of time	Rather less than I did		1
1		Not too often	Definitely less than I used to		2
0		Very little	Hardly at all		3
		I feel cheerful	**I get a sudden feeling of panic**		
	3	Never	Very often indeed	3	
	2	Not often	Quite often	2	
	1	Sometimes	Not very often	1	
	0	Most of the time	Not at all	0	
		I can sit at ease and feel relaxed	**I can enjoy a good book or radio or television programme**		
0		Definitely	Often		0
1		Usually	Sometimes		1
2		Not often	Not often		2
3		Not at all	Very seldom		3

LSAS

Fill out the following questionnaire with the most suitable answer listed below. Base you answers on you experience in the past week and, if you have complete the scale previously, be as consistent as possible in your perception of the situation described. Be sure to answer all items.

Fear or Anxiety:
0 = None
1 = Mild
2 = Moderate
3 = Severe

Avoidance:
0 = Never (0%)
1 = Occasionally (1—33%)
2 = Often (33—67%)
3 = Usually (67—100%)

	Fear or Anxiety	Avoidance
1. Telephoning in public		
2. Participating in small groups		
3. Eating in public places		
4. Drinking with others in public places		
5. Talking to people in authority		
6. Acting, performing or giving a talk in front of an audience		
7. Going to a party		
8. Working while being observed		
9. Writing while being observed		
10. Calling someone you don't know very well		
11. Talking with people you don't know very well		
12. Meeting strangers		
13. Urinating in a public bathroom		
14. Entering a room when others are already seated		
15. Being the centre of attention		
16. Speaking up at a meeting		
17. Taking a written test		
18. Expressing appropriate disagreement or disapproval to people you don't know very well		

19. Looking at people you don't know very well in the eyes		
20. Giving a report to a group		
21. Trying to pick up someone		
22. Returning goods to a store where returns are normally accepted		
23. Giving an average party		
24. Resisting a high pressure salesperson		

SRS-2

For each question, please circle the answer that best describes your behaviour over the past 6 months.

1 = NOT TRUE 2 = SOMETIMES TRUE 3 = OFTEN TRUE 4 = ALMOST ALWAYS TRUE

1. I am much more uncomfortable in social situations than when I am by myself.	1	2	3	4
2. My facial expressions send the wrong message to others about how I actually feel.	1	2	3	4
3. I feel self-confident when interacting with others.	1	2	3	4
4. When under stress, I engage in rigid or inflexible patterns of behaviour that seem odd to people.	1	2	3	4
5. I do not recognize when others are trying to take advantage of me.	1	2	3	4
6. I would rather be alone than with others.	1	2	3	4
7. I am usually aware of how others are feeling.	1	2	3	4
8. I behave in ways that seem strange or bizarre to others.	1	2	3	4
9. I am overly dependent on others for help with meeting my everyday needs.	1	2	3	4
10. I take things too literally, and because of that, I misinterpret the intended meaning of parts of a conversation.	1	2	3	4
11. I have good self-confidence.	1	2	3	4
12. I am able to communicate my feelings to others.	1	2	3	4
13. I am awkward in turn taking interactions with others (for example, I have a hard time keeping up with the give-and-take of a conversation.	1	2	3	4
14. I am not well coordinated.	1	2	3	4
15. When people change their tone or facial expression, I usually pick up on that and understand what it means.	1	2	3	4
16. I avoid eye contact or am told that I have unusual eye contact.	1	2	3	4
17. I recognise when something is unfair.	1	2	3	4

18. I have difficulty making friends, even when I'm trying my best.	1	2	3	4
19. I get frustrated trying to get ideas across in conversations.	1	2	3	4
20. I have sensory interests that others find unusual (for example, smelling or looking at things in a special way).	1	2	3	4
21. I am able to imitate others' actions and expressions when it is socially acceptable to do so.	1	2	3	4
22. I interact appropriately with other adults.	1	2	3	4
23. I do not join group activities or social events unless prompted or strongly urged to do so.	1	2	3	4
24. I have more difficulty than others with changes in my routine.	1	2	3	4
25. I do not mind being out of step with or "not on the same wavelength" as others.	1	2	3	4
26. I offer comfort to others when they are sad.	1	2	3	4
27. I avoid starting social interactions with other adults.	1	2	3	4
28. I think or talk about the same thing over and over.	1	2	3	4
29. I am regarded by others as odd or weird.	1	2	3	4
30. I become upset in situations with lots of things going on.	1	2	3	4
31. I can't get my mind off something once I started thinking about it.	1	2	3	4
32. I have good personal hygiene.	1	2	3	4
33. My behaviour is socially awkward, even when I'm trying to be polite.	1	2	3	4
34. I avoid people who want to be emotionally close to me.	1	2	3	4
35. I have trouble keeping up with the flow of normal conversation.	1	2	3	4
36. I have difficulty relating to family members.	1	2	3	4
37. I have difficulty relating to adults outside of my family.	1	2	3	4
38. I respond appropriately to mood changes in others (for example, when a friend's mood changes from happy to sad).	1	2	3	4
39. People think I am interested in too few topics, or that I get carried away with those topics.	1	2	3	4
40. I am imaginative.	1	2	3	4

41. I sometimes seem to wander aimlessly from one activity to another.	1	2	3	4
42. I am overly sensitive to certain sounds, textures, or smells.	1	2	3	4
43. I enjoy small talk (casual conversation with others).	1	2	3	4
44. I have more trouble than most people with understanding chains of causation (in other words, how events are related to one another).	1	2	3	4
45. When others around me are paying attention to something, I get interested in what they are attending to.	1	2	3	4
46. Others feel that I have overly serious facial expressions.	1	2	3	4
47. I laugh at inappropriate times.	1	2	3	4
48. I have a good sense of humor and can understand jokes.	1	2	3	4
49. I do extremely well at certain kinds of intellectual tasks, but do not do as well at most other tasks.	1	2	3	4
50. I have repetitive behaviours that others consider odd.	1	2	3	4
51. I have difficulty answering questions directly and end up talking around the subject.	1	2	3	4
52. I get overly loud without realizing it.	1	2	3	4
53. I tend to talk in a monotone voice (in other words, less inflection of voice than most people demonstrate).	1	2	3	4
54. I tend to think about people in the same way I do objects.	1	2	3	4
55. I get too close to others of invade their personal space without realizing it.	1	2	3	4
56. I sometimes make the mistake of walking between two people who are trying to talk to one another.	1	2	3	4
57. I tend to isolate myself.	1	2	3	4
58. I concentrate too much on parts of things rather than seeing the whole picture.	1	2	3	4
59. I am more suspicious than most people.	1	2	3	4
60. Other people think I am emotionally distant and do not show my feelings.	1	2	3	4
61. I tend to be inflexible.	1	2	3	4

62. When I tell someone my reason for doing something, it strikes the person as unusual or illogical.	1	2	3	4
63. My way of greeting another person is unusual.	1	2	3	4
64. I am much more tense in social settings than when I am by myself.	1	2	3	4
65. I find myself staring or gazing off into space.	1	2	3	4

TAS-20

		Disagree strongly	Somewhat disagree	Neutral	Somewhat agree	Agree strongly
1	I am often confused about what emotion I am feeling	1	2	3	4	5
2	It is difficult for me to find the right words for my feelings	1	2	3	4	5
3	I have physical sensations that even doctors don't understand	1	2	3	4	5
4	I am able to describe my feelings easily	1	2	3	4	5
5	I prefer to analyse problems rather than just describe them	1	2	3	4	5
6	When I am upset, I don't know if I am sad, frightened or angry	1	2	3	4	5
7	I am often puzzled by sensations in my body	1	2	3	4	5
8	I prefer to just let things happen rather than to understand why they turned out that way	1	2	3	4	5
9	I have feelings that I can't quite identify	1	2	3	4	5
10	Being in touch with emotions is essential	1	2	3	4	5
11	I find it hard to describe how I feel about people	1	2	3	4	5
12	People tell me to describe my feelings more	1	2	3	4	5
13	I don't know what's going on inside me	1	2	3	4	5
14	I often don't know why I am angry	1	2	3	4	5
15	I prefer talking to people about their daily activities rather than their feelings	1	2	3	4	5
16	I prefer to watch "light" entertainment shows rather than psychological dramas	1	2	3	4	5

17	It is difficult for me to reveal my innermost feelings, even to close friends	1	2	3	4	5
18	I can feel close to someone, even in moments of silence	1	2	3	4	5
19	I find examination of my feelings useful in solving personal problems	1	2	3	4	5
20	Looking for hidden meanings in movies or plays distracts from their enjoyment	1	2	3	4	5

WSAS

Please circle the number which best describes how you feel about each of these statements. If you are not currently experiencing any physical or mental health problems, please answer the questions anyway.

1. Because of my illness, my ability to work is impaired.

0	1	2	3	4	5	6	7	8
Not at all		Slightly		Definitely		Markedly		Very severely

2. Because of my illness, my home management (cleaning, tidying, shopping, cooking, looking after home or children, paying bills) is impaired.

0	1	2	3	4	5	6	7	8
Not at all		Slightly		Definitely		Markedly		Very severely

3. Because of my illness, my social leisure activities (with other people e.g. parties, bars, clubs, outings, visits, dating, home entertaining) are impaired.

0	1	2	3	4	5	6	7	8
Not at all		Slightly		Definitely		Markedly		Very severely

4. Because of my illness, my private leisure activities (done alone, such as reading, gardening, collecting, sewing, walking alone) are impaired.

0	1	2	3	4	5	6	7	8
Not at all		Slightly		Definitely		Markedly		Very severely

5. Because of my illness, my ability to form and maintain close relationships with others, including those I live with, is impaired.

0	1	2	3	4	5	6	7	8
Not at all		Slightly		Definitely		Markedly		Very severely